Baskar
09/769787

- key terms

FILE 'HCAPLUS' ENTERED AT 10:43:45 ON 05 SEP 2002)

L1 3049 SEA FILE=HCAPLUS ABB=ON PLU=ON ((STREPTOCOCC? OR S)(W)PNEUMON? OR STREPTOCOC?)(S)(TREAT? OR THERAP?)

L3 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L1(L)ANTAGONIST?

L3 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:586499 HCAPLUS

TITLE: Defense against biologic warfare with superantigen toxins

AUTHOR(S): Kaempfer, Raymond; Arad, Gila; Levy, Revital; Hillman, Dalia

CORPORATE SOURCE: Department of Molecular Virology, Hebrew University-Hadassah Medical School, Jerusalem, Israel

SOURCE: Israel Medical Association Journal (2002), 4(7), 520-523
CODEN: IMAJCX; ISSN: 1565-1088

PUBLISHER: Israel Medical Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Superantigens produced by Staphylococcus aureus and Streptococcus pyogenes are among the most lethal of toxins. Toxins in this family trigger an excessive cellular, immune response leading to toxic shock. Objectives: To design an **antagonist** that is effective in vivo against a broad spectrum of superantigen toxins. Methods: Short peptide **antagonists** were selected for their ability to inhibit superantigen-induced expression of human genes for cytokines that mediate shock. The ability of these peptides to protect mice against lethal toxin challenge was examd. Results: **Antagonist** peptide protected mice against lethal challenge with staphylococcal enterotoxin B and toxic shock syndrome toxin-1, superantigens that share only 6% overall amino acid homol. Moreover, it rescued mice undergoing toxic shock. **Antagonist** peptides show homol. to a .beta.-strand/hinge/.alpha.-helix domain that is structurally, conserved among superantigens, yet remote from known binding sites for the major histocompatibility class II mol. and T cell receptor that function in toxic T cell hyperactivation. Conclusions: The lethal effect of superantigens can be blocked with a peptide **antagonist** that inhibits their action at the top of the toxicity cascade before activation of cells occurs. Superantigenic toxin **antagonists** may serve not only as countermeasures to biol. warfare but may be useful in the **treatment** of staphylococcal and **streptococcal** toxic shock, as well as in some cases of septic shock.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:757814 HCAPLUS

DOCUMENT NUMBER: 135:298819

TITLE: Meta-substituted acidic 8-phenylxanthine antagonists of A3 human adenosine receptors, and their therapeutic use

INVENTOR(S): Linden, Joel M.

PATENT ASSIGNEE(S): University of Virginia, USA; University of Virginia Patent Foundation

SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6303619	B1	20011016	US 1998-38991	19980312

OTHER SOURCE(S): MARPAT 135:298819

AB The invention concerns the use of a xanthine or xanthine deriv. having a meta-substituted acidic aryl at the 8-position to specifically modulate the physiol. role of adenosine activation of its various receptors.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:824388 HCAPLUS
DOCUMENT NUMBER: 134:14738
TITLE: RNase P from Staphylococcus aureus and its sequence and solution structure and use for identifying antagonists for treatment of antibacterial infections
INVENTOR(S): Lehr, Ruth V.; Spitzfaden, Claus; Nicholson, Neville; Jones, Joanna
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000070025	A1	20001123	WO 2000-US13946	20000519
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1183333	A1	20020306	EP 2000-932665	20000519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1999-134802P P 19990519
US 1999-140044P P 19990618
WO 2000-US13946 W 20000519

AB This invention relates to a novel bacterial ribonucleoprotein complex and the component parts thereof. More specifically, this invention relates to RNase P protein and RNA isolated from Staphylococcus aureus and the use of RNase P RNA in screens for the identification of antimicrobial compds. and to the use of such compds. in therapy. The spp gene encoding the protein subunit of S. aureus RNase P was cloned and identified on the basis of amino acid sequence homol. with Bacillus subtilis and related bacterial RNase P proteins. RNase protein employs 2 different modes of RNA

interactions, which occupy distinct areas. NMR spectroscopy identifies a contiguous interaction site for flexible, single-strand RNA mols., representative of the 5'-leader sequence. Binding at this site is dominated by electrostatic charge and hydrogen bonding interactions, including main chain hydrogen bonds at the edge of the .beta.-sheet. The arginine-rich motif of RNase P protein does not bind to single-stranded RNA and is therefore likely to be responsible for the binding to the highly structured P RNA component. Given the essentiality of RNase P for the viability of the organism, knowledge of the S. aureus protein structure and insight into its interaction with RNA will help in the development of RNase P and its protein subunit as targets for novel antibiotics against this important pathogen.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:783948 HCAPLUS
DOCUMENT NUMBER: 132:9042
TITLE: Receptor ligand antagonist complexes and their use in treating or preventing receptor-mediated diseases
INVENTOR(S): Devico, Anthony L.; Lewis, George K.; Burns, Jennifer M.; Gallo, Robert
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962535	A2	19991209	WO 1999-US12137	19990601
WO 9962535	A3	20010329		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9943254	A1	19991220	AU 1999-43254	19990601
EP 1100527	A2	20010523	EP 1999-955219	19990601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6399078	B1	20020604	US 1999-323719	19990601

PRIORITY APPLN. INFO.: US 1998-87436P P 19980601
WO 1999-US12137 W 19990601

AB The invention provides therapeutic compns. of receptor ligand-contg. antagonist complexes and methods of using them to treat diseases, disorders or conditions assocd. with the function or aberrant function of a cell surface receptor.

L3 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:721870 HCAPLUS
DOCUMENT NUMBER: 132:30373
TITLE: Efficacy of levofloxacin for experimental aortic-valve endocarditis in rabbits infected with viridans group streptococcus or Staphylococcus aureus
AUTHOR(S): Chambers, Henry F.; Liu, Qing Xiang; Chow, Lucian Liuxin; Hackbarth, Corinne
CORPORATE SOURCE: Department of Medicine, University of California, San Francisco, CA, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(11), 2742-2746
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Levofloxacin is among the more active fluoroquinolones against streptococci and staphylococci. It is effective against moderately severe infections caused by these organisms, but its efficacy in the treatment of bacteremia and serious infections such as endocarditis is not well defined. We compared the efficacy of levofloxacin to those of std. agents in the rabbit model of aortic-valve endocarditis caused by fluoroquinolone-susceptible strains including a penicillin-susceptible strain of Streptococcus sanguis, a penicillin-resistant strain of Streptococcus mitis, a methicillin-resistant strain of Staphylococcus aureus, and a methicillin-susceptible strain of S. aureus. Levofloxacin administered i.m. at dosages of 20 to 40 mg/kg of body wt. twice daily (b.i.d.) was completely ineffective against the penicillin-susceptible strain, with mean vegetation titers after 3 days of therapy not statistically significantly different from those for controls. Levofloxacin was no more effective than penicillin against the penicillin-resistant strain. Levofloxacin administered for 4 days at a dosage of 20 mg/kg b.i.d. was at least as effective as vancomycin administered i.v. at a dosage of 25 mg/kg b.i.d. against the methicillin-resistant S. aureus strain and was as effective as nafcillin administered i.m. at 100 mg three times daily against the methicillin-susceptible strain. Emergence of resistance to levofloxacin in vitro was less likely to occur than resistance to ciprofloxacin, and resistance to levofloxacin was not obsd. in vivo. Levofloxacin-rifampin combinations were **antagonistic** in vitro and in vivo. Levofloxacin was highly effective as a single agent against exptl. staphylococcal endocarditis but was surprisingly ineffective against **streptococcal** endocarditis, suggesting that it has a potential role as **treatment** for serious S. aureus but not viridans group **streptococcal** infections in humans.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:549143 HCAPLUS
DOCUMENT NUMBER: 131:165336
TITLE: Xanthine derivative antagonists of A2b human adenosine receptors, and therapeutic use thereof

INVENTOR(S): Linden, Joel M.
PATENT ASSIGNEE(S): University of Virginia, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942093	A2	19990826	WO 1999-US4009	19990224
WO 9942093	A3	19991028		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6117878	A	20000912	US 1998-27649	19980224
AU 9928759	A1	19990906	AU 1999-28759	19990224

PRIORITY APPLN. INFO.: US 1998-27649 A 19980224
WO 1999-US4009 W 19990224

AB 8-Phenylxanthines, 8-cycloalkylxanthines or 8-substituted xanthine derivs. are used to specifically modulate the physiol. role of the A2B adenosine receptor. A compd. of the invention is e.g. enprofylline. The compds. of the invention are useful for e.g. blockage of inflammatory response and prevention of mast cell degranulation and can be used for the treatment of e.g. myocardial ischemia, asthma, or reperfusion injury.

L3 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:330111 HCAPLUS
DOCUMENT NUMBER: 131:15710
TITLE: Cloning of gene for xanthine phosphoribosyltransferase of Streptococcus pneumoniae and its clinical use
INVENTOR(S): Burnham, Martin Karl Russell; Black, Michael Terence; Hodgson, John Edward; Knowles, David Justin Charles; Lonetto, Michael Arthur; Nicholas, Richard Oakley; Stodola, Robert King
PATENT ASSIGNEE(S): Smith Klein Beecham Corporation, USA; Smithklein Beecham plc
SOURCE: Jpn. Kokai Tokkyo Koho, 62 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11137276	A2	19990525	JP 1998-236241	19980717

PRIORITY APPLN. INFO.: US 1997-896589 19970717

AB The Streptococcus pneumoniae homolog of the xanthine phosphoribosyltransferase gene of Bacillus subtilis is isolated. The deduced peptide sequence is comprised of 191 amino acids. Claimed are methods of recombinant prepn. of the gene product, use of the enzyme for developing diagnostics or **therapeutics** for diseases caused by **S. pneumoniae**, methods for vaccination of mammals with the enzyme protein, and methods of

screening agonists or **antagonists** of the enzyme protein.

L3 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:330110 HCAPLUS
DOCUMENT NUMBER: 131:15709
TITLE: Cloning of gene pcrA of Streptococcus pneumoniae and clinical use of the gene
INVENTOR(S): Holmes, David; Black, Michael Terence; Hodgson, John Edward; Knowles, David Justin Charles; Lonetto, Michael Arthur; Nicholas, Richard Oakly; Stodola, Robert King
PATENT ASSIGNEE(S): Smith Klein Beecham Corporation, Japan; Smithkline Beecham PLC
SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11137271	A2	19990525	JP 1998-229240	19980708
US 5858718	A	19990112	US 1997-889711	19970708
CA 2223008	AA	19980810	CA 1998-2223008	19980209
CA 2236473	AA	19990108	CA 1998-2236473	19980706
EP 890647	A2	19990113	EP 1998-305343	19980706
EP 890647	A3	20010919		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1997-889711 A 19970708
US 1997-37536P P 19970210

AB Gene pcrA of the DNA helicase family is isolated from Streptococcus pneumoniae. The deduced peptide sequence is comprised of 428 amino acids. Claimed are methods of recombinant prepn. of the gene product, use of pcrA protein for the diagnosis or **treatment** of diseases caused by **S. pneumoniae**, methods of vaccination of mammals with the pcrA protein, and methods of screening agonists or **antagonists** of the pcrA protein.

L3 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:260063 HCAPLUS
DOCUMENT NUMBER: 130:292454
TITLE: Nucleic acid molecule encoding Streptococcus pneumoniae histidine kinase, its DNA sequence and its biol., diagnostic, and immunol. uses
INVENTOR(S): Wallis, Nicola Gail; Zalacain, Magdalena; Brown, James Raymond
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 909820	A2	19990421	EP 1998-308075	19981005
EP 909820	A3	19990804		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6287836	B1	20010911	US 1997-947251	19971008
PRIORITY APPLN. INFO.:			US 1997-947251 A	19971008
			US 1997-48346P P	19970530
			US 1997-878858 B2	19970620

AB The invention provides Streptococcus pneumoniae histidine kinase polypeptides and DNA (RNA) encoding the histidine kinase polypeptides, and methods for producing histidine kinase by recombinant techniques. The DNA sequence of the S. pneumoniae histidine kinase gene, as well as the corresponding amino acid sequence for histidine kinase are claimed. The invention discloses methods for utilizing histidine kinase polynucleotides and polypeptides in biol., diagnostic, therapeutic and immunol. assays. Specifically, the invention discloses the use of **S. pneumoniae** histidine kinase in **treatment** of individuals in need of histidine kinase. In addn., the invention discloses the use of S. pneumoniae histidine kinase polynucleotides and polypeptides in diagnosis of diseases related to the expression or activity of histidine kinase. Further, the invention discloses the use of **S. pneumoniae** histidine kinase polypeptides in identifying agonists and/or **antagonists** of histidine kinase, and the use of identified **antagonists** in **treatment** of individuals needing to inhibit histidine kinase. Finally, the invention discloses the use of histidine kinase polypeptides or nucleic nucleic vectors contg. the histidine kinase gene in the induction of both humoral and T immune responses in mammals that protects the mammals from disease.

L3 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:7848 HCAPLUS
DOCUMENT NUMBER: 130:61059
TITLE: Inhibitors of microbial adherence or invasion as therapeutic agents and broad-spectrum enhancers of antibiotic therapy
INVENTOR(S): Cleary, Paul Patrick; Cue, David R.
PATENT ASSIGNEE(S): Regents of the University of Minnesota, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

WO 9856408	A2	19981217	WO 1998-US12019	19980610
WO 9856408	A3	19990304		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9879580 A1 19981230 AU 1998-79580 19980610
PRIORITY APPLN. INFO.: US 1997-49124P P 19970610
WO 1998-US12019 W 19980610

AB The invention is directed to therapeutic use of compds. that function as inhibitors of microbial intracellular invasion of or adherence to host mammalian cells. The compds. can either be an integrin antagonist (inhibition of the binding of fibronectin to .alpha.5.beta.1 integrin) or an invasin antagonist. The compds. could be a cyclic RGD-contg. peptide, a non-peptide or an antibody. The microbe could be a bacterial pathogen or a fungus. Co-administration of the inhibitory compd. with an antibiotic, such as penicillin that inefficiently permeates mammalian cell membranes, increases the efficacy of the antibiotic therapy.

L3 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:7847 HCAPLUS
DOCUMENT NUMBER: 130:61058
TITLE: Fibronectin antagonists as therapeutic agents and broad-spectrum enhancers of antibiotic therapy
INVENTOR(S): Cleary, Paul Patrick; Cue, David R.; Mousa, Shaker A.
PATENT ASSIGNEE(S): Regents of the University of Minnesota, USA; Dupont Pharmaceuticals Company
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856407	A2	19981217	WO 1998-US12010	19980610
WO 9856407	A3	19990304		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9880649 A1 19981230 AU 1998-80649 19980610
PRIORITY APPLN. INFO.: US 1997-49124P P 19970610
WO 1998-US12010 W 19980610

AB The invention is directed to therapeutic use of fibronectin antagonists to inhibit microbial intracellular invasion of or adherence to host mammalian cells by binding to the fibronectin receptors such as .alpha.5.beta.1 integrin. The fibronectin antagonists can be a cyclic RGD-contg. peptide, a non-peptide or an antibody. The microbe can be a bacterial pathogen such as Streptococcus of fungus such as Candida. Co-administration of the inhibitory compd. with an antibiotic, such as penicillin that inefficiently permeates mammalian cell membranes, increases the

efficacy of the antibiotic therapy.

L3 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180736 HCAPLUS
DOCUMENT NUMBER: 128:240357
TITLE: Novel tryptophanyl tRNA synthetase trpS proteins and genes and their use in screening antibacterial agents
INVENTOR(S): Gentry, Daniel Robert; Greenwood, Rebecca Claire; Lawlor, Elizabeth Jane
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA; Gentry, Daniel Robert; Greenwood, Rebecca Claire; Lawlor, Elizabeth Jane
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810652	A1	19980319	WO 1997-US16367	19970912
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5851809	A	19981222	US 1997-923867	19970904
EP 843014	A2	19980520	EP 1997-307007	19970910
EP 843014	A3	19991103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10215882	A2	19980818	JP 1997-289010	19970912
US 6046174	A	20000404	US 1997-928100	19970912
JP 2001501463	T2	20010206	JP 1998-513969	19970912
US 6165759	A	20001226	US 1998-183134	19981030
US 6416976	B1	20020709	US 1999-425666	19991022
US 6346409	B1	20020212	US 2000-492581	20000127

PRIORITY APPLN. INFO.:
GB 1996-19072 A 19960912
US 1997-923867 A3 19970904
US 1997-928100 A3 19970912
WO 1997-US16367 W 19970912

AB The invention provides tryptophanyl tRNA synthetase (trpS) polypeptides and DNA, cDNA, or RNA encoding trpS polypeptides and methods for producing such polypeptides by std. recombinant techniques. The trpS proteins have .gtoreq.70% sequence homol. to the tryptophanyl tRNA synthetases from Clostridium longisporum and Streptococcus pneumoniae. Antibodies and **antagonists** for trpS proteins are also claimed. The trpS proteins are frequent targets for antibacterial agents. Thus, methods are provided for utilizing trpS polypeptides to screen for novel antibacterial compds. These novel antibacterial compds. are useful for **treating S. pneumoniae** infections resistant to many std. antibiotics.

L3 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:776178 HCAPLUS
DOCUMENT NUMBER: 128:43839
TITLE: Use of kinin antagonists for preparing a

pharmaceutical composition for treating bacterial infections
INVENTOR(S): Bjorck, Lars; Sjobring, Ulf; Ben Nasr, Abdelhakim; Olsen, Arne; Herwald, Heiko; Muller-Esterl, Werner
PATENT ASSIGNEE(S): Actinova Ltd., UK; Bjorck, Lars; Sjobring, Ulf; Ben Nasr, Abdelhakim; Olsen, Arne; Herwald, Heiko; Muller-Esterl, Werner
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744353	A1	19971127	WO 1997-SE825	19970520
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729857	A1	19971209	AU 1997-29857	19970520
US 6242210	B1	20010605	US 1999-258688	19990226
US 6221845	B1	20010424	US 1999-194098	19990625

PRIORITY APPLN. INFO.:
SE 1996-1901 A 19960520
WO 1997-SE825 W 19970520
US 1999-194098 A1 19990625

AB Kinin **antagonists**, esp. bradykinin **antagonists**, can be used for **treating** bacterial infections, in particular infections caused by bacteria belonging to the genera **Streptococcus**, Escherichia, Salmonella, Staphylococcus, Klebsiella, Moracella, Haemophilus and Yersinia.

L3 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:468834 HCAPLUS
DOCUMENT NUMBER: 127:171306
TITLE: Signal transduction in the platelet activation induced by IgG anti-streptokinase and anisoylated plasminogen-streptokinase activator complex
AUTHOR(S): Abdelouahed, M.; Emadi, S.; Elalamy, I.; Samama, M. M.; Hatmi, M.
CORPORATE SOURCE: Unite de Pharmacologie Cellulaire, Unite Associee Institut Pasteur-INSERM, U285, Paris, 75724, Fr.
SOURCE: Platelets (1997), 8(2/3), 135-141
CODEN: PLTEEF; ISSN: 0953-7104
PUBLISHER: Carfax
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Streptokinase (SK) is one of the plasminogen activators currently used in therapeutics. SK antibodies may appear in the blood after thrombolytic **therapy** with SK or after .beta.-hemolytic

streptococci infection. Such antibodies may both activate platelets and neutralize the ability of SK to convert plasminogen into plasmin. We previously demonstrated that platelet activation induced by the combination of IgG anti-SK and anisoylated plasminogen-SK activator complex (APSAC) is mediated by Fc.gamma.RIIa1 receptor. However, the mechanism by which IgG anti-SK and APSAC (or SK) transduce an activating signal across the platelet plasma membrane remains unknown. We have demonstrated in the present study that the platelet aggregation induced by the combination of IgG anti-SK and APSAC is accompanied by an increase in inositol phosphate, Ca2+ mobilization and thromboxane (Tx) A2 generation. Neomycin, erbstatin and GF 109203X, which inhibit phospholipase C (PLC), protein tyrosine kinase (PTK) and protein kinase C (PKC) activities, resp., abolished platelet aggregation induced by IgG anti-SK plus APSAC, indicating the pivotal roles of the PLC, PTK and PKC pathways in this immunol. activation. In addn., TxA2 generation is also important since aspirin, a cyclo-oxygenase inhibitor and SQ 29548, a TxA2 receptor **antagonist**, showed significant inhibition of the platelet response. The contribution of released ADP was confirmed using apyrase, which significantly inhibited IgG anti-SK plus APSAC-induced platelet aggregation. Finally, WEB 2086, a platelet-activating factor (PAF) receptor **antagonist**, was not effective, indicating that PAF is not involved in this process. APSAC- or SK-induced platelet activation may limit the therapeutic effectiveness of the drug and may contribute to the pathogenesis of early reocclusion. The study of the mechanism leading to APSAC-induced platelet activation could be relevant for a better understanding of the physiopathol. of immune complex disorder diseases and thrombolytic treatment failure.

L3 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:181148 HCAPLUS
DOCUMENT NUMBER: 126:170399
TITLE: IL-8 antagonists for treatment of inflammatory disorders and asthma
INVENTOR(S): Hebert, Caroline A.; Kabakoff, Rhona C.; Moore, Mark W.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9701354	A1	19970116	WO 1996-US11033	19960626
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5874080	A	19990223	US 1995-491334	19950627
AU 9662924	A1	19970130	AU 1996-62924	19960626

AU 727343	B2	20001214			
EP 840620	A1	19980513	EP 1996-921804		19960626
EP 840620	B1	20011010			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11509840	T2	19990831	JP 1996-504031		19960626
AT 206621	E	20011015	AT 1996-921804		19960626
PRIORITY APPLN. INFO.:			US 1995-491334	A	19950627
			US 1994-205864	B2	19940303
			US 1995-398611	A2	19950301
			WO 1996-US11033	W	19960626

AB Methods are provided for the treatment of asthma with recombinant anti-IL-8 antibodies. Procedures for prodn. of chimeric mouse-human IL-8-specific monoclonal antibodies are detailed.

L3 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:183947 HCAPLUS
DOCUMENT NUMBER: 124:250801
TITLE: A novel nonpsychotropic cannabinoid, HU-211, in the treatment of experimental pneumococcal meningitis
AUTHOR(S): Bass, Roman; Engelhard, Dan; Trembovler, Victoria; Shohami, Esther
CORPORATE SOURCE: Departments Pharmacology and Pediatrics, Hebrew University, Jerusalem, 91120, Israel
SOURCE: Journal of Infectious Diseases (1996), 173(3), 735-8
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Typical features of pneumococcal meningitis have been demonstrated in rats inoculated with Streptococcus pneumoniae. HU-211, a novel noncompetitive N-methyl-D-aspartate **antagonist** recently demonstrated to inhibit tumor necrosis factor-.alpha. prodn. under various conditions, improves recovery in some exptl. models of brain injury. The present study tested the efficacy of HU-211 in combination with antimicrobial therapy in reducing brain damage in exptl. pneumococcal meningitis. **S. pneumoniae** -infected rats were **treated** with saline alone, ceftriaxone alone, or with a combination of ceftriaxone and HU-211 18 h after inoculation of the bacteria. Brain edema and blood-brain barrier impairment 48 h after infection were significantly ($P < .05$) reduced in rats treated with ceftriaxone-HU-211 compared with rats in other treatment groups. The results suggest that HU-211 when given concomitantly with antibiotics attenuates brain damage in the rat model of pneumococcal meningitis.

L3 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:896627 HCAPLUS
DOCUMENT NUMBER: 123:329976
TITLE: Modulators of pneumococcal adhesion to cellular targets involving the platelet-activating factor receptor and their uses
INVENTOR(S): Tuomanen, Elaine I.; Cundell, Diana R.; Gerard, Norma P.
PATENT ASSIGNEE(S): Rockefeller University, USA; Beth Israel Hospital Association

SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5455240	A	19951003	US 1994-262306	19940620
WO 9535112	A2	19951228	WO 1995-US7687	19950619
WO 9535112	A3	19960201		
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, IS, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, TM, UA, UG, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2193362	AA	19951228	CA 1995-2193362	19950619
AU 9527758	A1	19960115	AU 1995-27758	19950619
AU 701347	B2	19990128		
EP 762884	A1	19970319	EP 1995-923082	19950619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504535	T2	19980506	JP 1995-502513	19950619

PRIORITY APPLN. INFO.: US 1994-262306 19940620
WO 1995-US7687 19950619

AB Compns. and methods are disclosed for preventing pneumococcal infection. In particular, the invention relates to identification of the major receptor for **Streptococcus pneumoniae** on activated human cells, and diagnostic and **therapeutic** compns. and methods based thereon. In particular, the invention relates to the discovery that platelet-activating factor (PAF) receptor is an adhesive ligand for pneumococcal adherence to activated lung epithelial and venous endothelial (i.e., host) cells. Accordingly, the present invention is directed to a method for preventing or **treating** an infection with **Streptococcus pneumoniae** by administering an **antagonist** of PAF receptor. The invention further relates to recognition that adherence to activated cells also involves a carbohydrate ligand found on such activated cells. Thus, a method for inhibiting pneumococcal adherence may further comprise administering an amt. of carbohydrate contg. an N-acetyl-D-glucosamine motif. It has been found that resting lung epithelial and venous endothelial cells bear two classes of receptors contg. different carbohydrate motifs. Thus, the invention further provides for administering an amt. of a second carbohydrate selected from the group consisting of a carbohydrate contg. a disaccharide N-acetyl-D-galactosamine .beta.1-4Gal motif, a disaccharide N-acetyl-D-galactosamine .beta.1-3Gal motif, and a mixt. thereof. In addn., the invention provides pharmaceutical compns. comprising such agents that inhibit binding of pneumococci to human cells. In a specific example, PAF receptor **antagonists** and disaccharides are shown to inhibit binding of pneumococci to activated lung epithelial cells and venous endothelial cells, as well as cells transfected with the PAF receptor, in vitro.

L3 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:623075 HCAPLUS

DOCUMENT NUMBER: 119:223075
TITLE: Killing of endothelial cells and release of arachidonic acid: synergistic effects among hydrogen peroxide, membrane-damaging agents, cationic substances, and proteinases and their modulation by inhibitors
AUTHOR(S): Ginsburg, Isaac; Mitra, Raj S.; Gibbs, Douglas F.; Varani, James; Kohen, Roni
CORPORATE SOURCE: Dep. Oral Biol., Hebrew University-Hadassah Sch. Med., Jerusalem, 91-010, Israel
SOURCE: Inflammation (N. Y.) (1993), 17(3), 295-319
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 51Cr-labeled rat pulmonary artery endothelial cells (EC) cultivated in min. Eagle's medium were killed, in a synergistic manner, by mixts. of subtoxic amts. of glucose oxidase-generated H2O2 and subtoxic amts. of the following agents: the cationic substances, nuclear histone, defensins, lysozyme, poly-L-arginine, spermine, pancreatic RNase, polymyxin B, chlorhexidine, cetyltrimethyl ammonium bromide; as well as by the membrane-damaging agents phospholipases A2 (PLA2) and C (PLC), lysolecithin (LL), and streptolysin S (SLS) of group A streptococci. Cytotoxicity induced by such mixts. was further enhanced by subtoxic amts. either of trypsin or of elastase. Glucose-oxidase cationized by complexing to poly-L-histidine proved an excellent deliverer of membrane-directed H2O2 capable of enhancing EC killing by other agonists. EC **treated** with rabbit anti-**streptococcal** IgG were also killed, in a synergistic manner, by H2O2, suggesting the presence in the IgG prepn. of cross-reactive antibodies. Killing of EC by the various mixts. of agonists was strongly inhibited by scavengers of H2O2 (catalase, dimethylthiourea, MnCl2), soybean trypsin inhibitor, polyanions, and putative inhibitors of phospholipases. Strong inhibition of cell killing was also given by tannic acid and by exts. of tea, but less so by serum. On the other hand, neither deferoxamine, HClO, tumor necrosis factor, nor GTP.gamma.S had any modulating effects on the synergistic cell killing. EC exposed either to 6-deoxyglucose, puromycin, or trifluprom azine became highly susceptible to killing by mixts. of H2O2 peroxide with several of the membrane-damaging agents. While maximal synergistic EC killing was achieved by mixts. of H2O2 with either PLA2, PLC, LL, or SLS, a very substantial release of [3H]-arachidonic acid (AA), PGE2, and 6-keto-PGF occurred only if a proteinase was also added to the mixt. of agonists. The release of AA from EC was markedly inhibited either by scavengers of H2O2, by proteinase inhibitors, by cationic agents, by HClO, by tannic acid, and by quinacrine. It is suggested that cellular injury induced in inflammatory and infectious sites might be the result of synergistic effects among leukocyte-derived oxidants, lysosomal hydrolases, cytotoxic cationic polypeptides, proteinases, and microbial toxins, which might be present in exudates. These "cocktails" not only kill cells, but also solubilize AA and several of its metabolites. However, AA release by the various agonists can be also achieved following attack by leukocyte-derived agonists on dead cells. It is proposed that treatment by "cocktails" of adequate **antagonists** might be beneficial in protecting against cellular injury in vivo.

L3 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:400323 HCAPLUS
DOCUMENT NUMBER: 107:323
TITLE: Antimicrobial alternatives for calf diarrhea: enteric responses to Escherichia coli, deferoxamine, or gallium in neonatal calves
AUTHOR(S): Fettman, Martin J.; Brooks, Patricia A.; Jones, Robert L.; Mero, Kendall N.; Phillips, Robert W.
CORPORATE SOURCE: Coll. Vet. Med. Biomed. Sci., Colorado State Univ., Fort Collins, CO, 80523, USA
SOURCE: Am. J. Vet. Res. (1987), 48(4), 569-77
CODEN: AJVRAH; ISSN: 0002-9645
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two iron **antagonists** were studied for their potential as alternative antimicrobials for E. coli diarrhea. Deferoxamine, a fungal iron chelator used to treat acute iron intoxication, and elemental Ga, a competitive inhibitor of iron activity in metabolic enzyme systems, were examd. for their effects on enteric morphol. and function in neonatal calves. Twelve male calves were allotted to 4 groups: (1) given nonpathogenic E. coli (control; (2) given enterotoxigenic B44 E. coli; (3) given deferoxamine (50 mg/kg, twice a day); and (4) given Ga (4 mg/kg, twice a day). Calves were studied for 8 days, including the conduct of oral glucose and lactose tolerance tests on days 1, 3, and 7. By day 7, according to oral glucose and lactose tolerance tests, peak plasma glucose concns. in all calves of groups 2, 3, and 4 were lower than those values in controls. The frequency of diarrhea was significant in all treated calves, and disease was most severe in the deferoxamine-treated calves. Quant. cultural examn. on day 8 showed significant numerical increases of jejunal and ileal E. coli and ileal lactobacilli in deferoxamine-**treated** calves (group 3) and of ileal **streptococci** in Ga-**treated** calves (group 4) and showed jejunal and ilea overgrowths of Saccharomyces yeast in deferoxamine-**treated** calves. Histopathol. ranking of intestinal sections obtained on day 8 revealed more severe lesions in treated (groups 2, 3, and 4) vs. control (group 1) calves and Ga-treated (group 4) vs. E. coli-inoculated (group 2) calves. Alterations in enteric flora, morphol., and function indicated that, at the doses used in the present study, the 2 iron **antagonists** would not provide an efficacious alternative therapeutic approach.

L3 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:117959 HCAPLUS
DOCUMENT NUMBER: 90:117959
TITLE: Formation of fermentation products by Streptococcus diacetilactis 639-1 culture and its antagonistically active mutants
AUTHOR(S): Sidorova, I. N.; Zaborskikh, E. I.; Kagan, Ya. R.
CORPORATE SOURCE: USSR
SOURCE: Biol. Mikroorg. Ikh Ispol'z. Nar. Khoz. (1977), 94-8. Editor(s): Grinevich, A. G. Irkutskii Univ.: Irkutsk, USSR.
CODEN: 40BYAV
DOCUMENT TYPE: Conference
LANGUAGE: Russian

AB **Treatment** of **Streptococcus** diacetylactis with nitrosomethylurea or di-Me sulfate produced various mutants which inhibited the growth of Escherichia coli, Staphylococcus aureus and other test organisms. Cultivation of S. diacetilactis parent strain in sterile skim milk resulted in the formation of diacetyl, acetoin, and volatile acids. Max. accumulation of these products occurred after 24 h of incubation. Cultivation of the **antagonistic** mutants under the same conditions resulted in accumulation of higher amts. of diacetyl and acetoin but similar quantities of volatile acids. No clear correlation was found between the fermn. products and the antimicrobial (**antagonistic**) properties of the mutants.

L3 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:435798 HCAPLUS
DOCUMENT NUMBER: 87:35798
TITLE: Increased antagonistic activity of lactic streptococci under the effect of mutagenic factors
AUTHOR(S): Zaborskikh, E. I.
CORPORATE SOURCE: USSR
SOURCE: Biol. Mikroorg. Ikh Ispol'z. Nar. Khoz. (1975), 2, 50-9
CODEN: BMIKDY
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Streptococcus lactis, S. diacetilactis, and S. paracitrovorus inhibited the growth of Escherichia coli in vitro. The **antagonistic** activity of **streptococci** was enhanced 2-2.5-fold after UV irradn. or **treatment** with dimethyl sulfate and nitrosomethylurea.

L3 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1954:71803 HCAPLUS
DOCUMENT NUMBER: 48:71803
ORIGINAL REFERENCE NO.: 48:12783e-i,12784a-i,12785a-i,12786a-i
TITLE: Analogs of pteroylglutamic acid. IX. Derivatives with substituents on the benzene ring
AUTHOR(S): Cosulich, Donna B.; Seeger, Doris R.; Fahrenbach, Marvin J.; Collins, Kenneth H.; Roth, Barbara; Hultquist, Martin E.; Smith, James M., Jr.
CORPORATE SOURCE: American Cyanamid Co., Bound Brook, NJ
SOURCE: J. Am. Chem. Soc. (1953), 75, 4675-80
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 46, 3060h, 5055b. A series of pteroylglutamic acid derivs. has been synthesized with halogen and Me substituents in the benzene ring moiety. The nitration of pteroylglutamic acid (I) and its 4-H2N deriv. (II) has been investigated. A no. of new nitrobenzoic and nitrobenzoylglutamic acid derivs. have been synthesized as intermediates and reference compds. I (4.9-g.) in 44 cc. concd. HCl and 44 cc. H2O treated at 15.degree. with 3.26 g. ICl, the mixt. warmed gently to 30.degree., cooled, let stand overnight, the resulting ppt. filtered off, washed with 5N HCl, dissolved in 30 cc. concd. HCl, dild. with 30 cc. H2O, the thick slurry cooled, filtered, washed with 5N HCl, pptd. in the same manner, the ppt. slurried in 250 cc. H2O, adjusted with NaOH to about pH 2.5, and the

somewhat gelatinous ppt. filtered off, washed with H2O, and dried yielded 3.2 g. crude 3-iodopteroylglutamic acid (III), .lambda.max. 255, 280, 365 m.mu., .lambda.min. 243, 270, 321 m.mu.. In a similar run with 49 g. I, was obtained 48.5 g. III. Crude III (45 g.) in 500 cc. H2O adjusted with NaOH to pH 11, and the soln. gradually acidified with AcOH gave a gel; a small part of the gel treated with 5N HCl gave a purplish brown mass with the liberation of iodine; another portion treated with an equal vol. of Me2CO and then with 5N HCl to give a clear, dark yellow soln., and the soln. adjusted to pH 3-4 with 5N NaOH gave a yellow ppt. of III which was washed with H2O and Me2CO and dried. (4-Aminobenzoyl)glutamic acid (IV) (26.6 g.) in 250 cc. H2O treated with stirring during 10 min. with 32.48 g. ICl, the purple ppt. filtered off, reslurried in 500 cc. H2O contg. 25 g. KI, filtered, washed with H2O, dissolved in 500 cc. dil. aq. NaOH at pH 11.5, the soln. treated with a little NaHSO3, stirred with activated C, filtered, acidified, and the yellow gum which quickly solidified filtered off, washed, and recrystd. from aq. EtOH gave 25 g. (4-amino-3,5-diiodobenzoyl)glutamic acid, m. 224.5.degree. (decompn.). IV (532 g.) in 3 l. hot H2O treated with 240 cc. 50% aq. NaOH, the soln. cooled to 10-20.degree., treated slowly with 262 g. EtO2-CCl together with sufficient NaOH to keep the soln. alk., acidified with concd. HCl to about pH 2.5-3.0, cooled, filtered, the residual Na salt of (4-carbethoxyaminobenzoyl)glutamic acid (V) dissolved in 1 l. H2O, decolorized with activated C, acidified to pH 1, let stand overnight, and the cryst. product filtered off, washed with H2O, EtOH, and C6H6, and dried at 50.degree. yielded 390 g. (57.5%) V, m. 173.0-5.0.degree.; recrystd. several times from H2O, it m. 174.5-7.5.degree.. In a similar run with 7.5 times the amt. of material the yield of V was 72%. To 7.48 cc. 70% HNO3 and 13.52 cc. concd. H2SO4 was added slowly at 0-5.degree. 3.38 g. V, the mixt. poured after 1 hr. into ice and H2O, and the white gelatinous ppt. filtered off, washed, dried (5 g.), and recrystd. from H2O, yielding 1.5 g. (4-carbethoxyamino-3,5-dinitrobenzoyl)glutamic acid (VI), m. 203.5-204.degree.. VI treated with dil. NaOH gave low yields of a product, m. 196-218.degree., which was not further identified. Hydrolysis of VI in hot 2N H2SO4 gave 4,3,5-H2N(O2N)2C6H2CO2H, m. 255-6.degree.. I (4.9 g.) in 30 cc. concd. H2SO4 **treated** at 0.degree. 2-3 min. with 1.87 cc. 70% HNO3, the mixt. poured on crushed ice, the yellow ppt. redissolved by warming to 40.degree. and adding a little H2O, the soln. clarified with activated C, adjusted with NaOH to pH 1, cooled to 8.degree., and the ppt. filtered off, washed with H2O, and dried gave 3.3 g. yellow material having 0.22% I activity as a growth factor for **Streptococcus** faecalis; 0.773 g. of the material slurried in 530 cc. H2O and dissolved with the min. amt. of NaOH on the steam bath, the hot soln. added slowly to 265 cc. 30% AcOH, clarified, cooled, and the resulting small spherulites filtered off and dried gave 0.46 g. about 80% pure 3,5-dinitropteroylglutamic acid (VII), crystg. with 1 mole H2O, .lambda.max. 258, 367, .lambda.min. 312 m.mu.. O passed 16 hrs. through 2 g. VII in 200 cc. N NaOH at 95-100.degree., the cooled soln. adjusted to pH 3, and the ppt. centrifuged off, washed 3 times with H2O and once with Me2CO, and dried gave 0.52 g. 2-amino-4-hydroxy-6-pteridinecarboxylic acid; the supernatant liquid and the washings combined, evapd. in vacuo to 50 cc., the concd. soln. cooled, the white ppt. extd. with cold Me2CO, and the ext. evapd. yielded 0.185 g. (4-amino-3,5-dinitrobenzoyl)glutamic acid, needles, m. 140-75.degree.. VII (2 g.) and 200 cc. 2N H2SO4

refluxed overnight under N, and the insol. material filtered off, washed with H2O and Me2CO, and dried gave 0.842 g. 2-amino-4-hydroxy-6-pteridinecarboxaldehyde; the Me2CO wash evapd. gave a very small amt. of gummy material; the main acid filtrate adjusted to about pH 3 and cooled, and the ppt. filtered off, washed with Me2CO, and dried gave 0.18 g. material, .lambda.max. 368 m.mu., which was not further identified; the filtrate evapd. to dryness in vacuo, the residue extd. with Me2CO, the insol. residue extd. with boiling EtOH, and the alc. ext. concd. to a small vol. and dild. with H2O gave 0.355 g. solid which, recrystd. twice from aq. EtOH, yielded 0.19 g. white feathery needles, m. 205.5-207.degree.. II (6.9 g.) nitrated similarly yielded 0.1374 g. 4-amino-3,5-dinitropteroylglutamic acid (VIII) crystg. with 3 moles H2O, .lambda.max. 256, 375, .lambda.min. 315 m.mu.. Into 476 g. V in 1400 cc. glacial AcOH and 140 cc. concd. HCl was passed slowly at 20-30.degree. 112 g. Cl, the excess Cl, HCl, and some AcOH distd. off in vacuo at 30-40.degree. during 0.5 hr., the remaining soln. dild. to 6 l. with with H2O, let stand several days at 0-5.degree., and the solid deposit filtered off, washed with H2O and a little EtOAc, and dried at 40.degree., yielding 425 g. (81.5 g.) 3-Cl deriv. (IX) of V, m. 158.5-61.0.degree. (recrystd. twice from H2O, m. 165.0-6.2.degree.); in a similar run with 6 times the amts. of material the yield of IX was 84.6%. IX (410 g.) in 1760 cc. 5N NaOH heated 3 hrs. at 50-60.degree., neutralized with HCl, clarified with activated C, acidified, the oily ppt. let stand overnight, and the resulting solid recrystd. from hot H2O contg. a little AcOH yielded 123 g. (41%)(4-amino-3-chlorobenzoyl)glutamic acid (X), m. 142-5.degree.; recrystd. 3 times from H2O, it m. 150.0-1.0.degree., [.alpha.]25D -11.3.degree. (c 2, 0.1N HCl). X (2 g.) boiled 10 min. in 20 g. 40% aq. NaOH, cooled, dild. with 25 cc. H2O, neutralized, decolorized with activated C, acidified, and the ppt. filtered off and recrystd. from 50% EtOH yielded 0.2 g. 3,4-Cl(H2N)C6H3CO2H, m. 225-7.degree.. X (15 g.), 25.4 g. 2,4,5-triamino-6-hydroxypyrimidine (XI) sulfate and 36.8 g. CHBr2COCH2Br (XII) gave 43 g. 10% 3'-chloropteroylglutamic acid (XIII), showing a low level of **antagonist** activity to folic acid. Crude material contg. 9.5 g. XIII dissolved in 5 l. 0.1N NaOH by heating 0.5 hr. at 70-5.degree., the soln. treated with 30% CaCl2, the mixt. filtered, the filtrate adjusted with 10% aq. ZnCl2 to pH 10.84, clarified, adjusted to pH 2.5, cooled, the ppt. filtered off, dissolved in 4 l. H2O contg. NaOH to give about pH 11, the soln. heated to 70.degree., adjusted to pH 7 while cooled to 20.degree., clarified, adjusted to pH 2.56, cooled, the ppt. filtered off, again dissolved in dil. aq. NaOH, treated with CaCl2 and ZnCl2, adjusted to pH 2.5, and the ppt. dried yielded 5.1 g. of 79.6% pure XIII, .lambda.max. 255, 278, 365, .lambda.min. 236, 270, 328 m.mu.. X (150 g.), 274 g. 2,4,5,6-tetraaminopyrimidine (XIV) sulfate, and 442 g. XII gave 1200 g. wet crude 4-amino-3'-chloropteroylglutamic acid (XV) (chem. assay 4.58%), which was purified in the usual manner to give 17.5 g. 85.4% pure XV, .lambda.max. 260,280, 369, .lambda.min. 240, 270, 330 m.mu.. 2,4-Cl(O2N)C6H3Me with alk. KMnO4 gave 53% 2,4-Cl(O2N)C6H3CO2H (XVI), m. 142-3.degree. (from H2O). XVI gave with PCl5 an oily product which contained some of the acid chloride since with NH4OH it yielded 2,4-Cl(O2N)C6H3CONH2, m. 166.degree.. XVI (80 g.) and 2400 cc. abs. MeOH treated cautiously with 32 cc. 100% H2SO4, refluxed 18 hrs., the MeOH distd. off, and the concentrate let crystallize, slurried in ice-water, and neutralized with NaHCO3 yielded 91-6% Me ester (XVII) of XVI, m.

75.5-6.7.degree.. XVII (78.4 g.) in 2400 cc. abs. MeOH treated slowly with 59.2 cc. N2H4.H2O, the mixt. let stand 18 hrs. at room temp. under N, most of the MeOH distd. off in vacuo, the residue poured into H2O, acidified with HCl, filtered, the filtrate neutralized, and the ppt. washed and dried gave 61.8 g. (79%) 2,4-Cl(O2N)C6H3CONHNH2 (XVIII), m. 156-7.degree.. XVIII (21.5 g.), 300 cc. cold H2O, 30 cc. glacial AcOH, 20 cc. concd. HCl, and 250 cc. iso-PrOAc treated during 10 min. at 0.degree. with 9.65 g. NaNO2 in 100 cc. H2O, the mixt. stirred 20 min. at 0.degree., the aq. layer extd. with 250 cc. iso-PrOAc, the combined ext. and org. layer washed with H2O, added to 130 g. di-Et glutamate sulfate in 200 cc. H2O previously neutralized with excess NaHCO3, the mixt. stirred 20 hrs. at room temp., the org. layer washed with H2O, dried, and evapd., and the crude solid residue redissolved in 100 cc. iso-PrOAc and dild. with 1000 cc. CCl4 and 1000 cc. petr. ether yielded 22.7 g. di-Et(2-chloro-4-nitrobenzoyl)glutamate (XIX), m. 98-8.5.degree.. XIX (4.8 g.) treated with 100 cc. 2N NaOH 24 hrs. at room temp., the soln. acidified, treated with 4.1 g. Zn dust, 0.5 g. CuSO4.5H2O, and 10 cc. H2O during 25 min. at 30-5.degree. with sufficient concd. HCl to maintain a pH of 3-4, the mixt. stirred 0.5 hr., and clarified, and the soln. (141 cc.), contg. a 95% yield of (4-amino-2-chlorobenzoyl)glutamic acid (titrated with nitrite), condensed with 7 g. XIV and 9.2 g. XII by the method of Hultquist and Dreisbach (C.A. 42, 7944b) yielded 7.6 g. 4-amino-2'-chloropteroylglutamic acid (XX) (chem. assay 23.7%), which was a very weak **antagonist** for I. Crude XX (6.5 g.) purified in the usual manner with CaCl2 and ZnCl2 yielded 0.413 g. 82% pure XX, .lambda.max. 260, 370, .lambda.min. 238, 325 m.mu.. 2,3,4-Cl2(O2N)C6H2Me (XXI) (43.3 g.) in 109 cc. concd. H2SO4 and 20.8 cc. H2O heated to 60-5.degree. and gradually treated during 1.5 hrs. at 62-5.degree. with 80.5 Na2Cr2O7, the resulting stiff mass thinned with 6 cc. H2O, stirred 1 hr. at 60-70.degree., cooled, dild. with 120 cc. H2O, the mixt. steam-distd. to give 20.5 g. (47.3%) recovered XXI, the residual hot aq. liquor decanted from a green gummy material, clarified, cooled, the ppt. filtered off, washed with H2O contg. a little HCl, dissolved in 200 cc. H2O with NaHCO3, the soln. clarified with activated C, acidified to about pH 1, cooled, and the ppt. washed and dried gave 5.7 g. 2,3,4-Cl2(O2N)C6H2CO2H (XXII), m. 127-46.degree.; purified by 3 pptns. from H2O, and drying at 102.degree., it m. 135.8-43.degree.. XXI oxidized with dil. HNO3 in a sealed tube at 140.degree. by the method of Cohen and Dakin (J. Chem. Soc. 81, 1347(1902)) gave 7-16% XXII with 30-60% recovery of XXI. XXII (1 g.) heated 0.5 hr. with 5 cc. SOCl2, the excess SOCl2 removed in vacuo, the residue extd. with hot petr. ether, the ext. evapd., the oily residue slowly added to 0.62 g. glutamic acid in 8.4 cc. N NaOH with addnl. NaOH to maintain a pH of 11, the mixt. let stand 1.5 hrs., heated to 70.degree., filtered, acidified, the waxy ppt. repptd. from aq. NaHCO3, and the resulting product (0.875 g.) repptd. 3 times more from aq. NaHCO3 and let stand in strongly acid soln. until crystd. gave 0.340 g. (2,3-dichloro-4-nitrobenzoyl)glutamic acid, m. 79-83.degree.. 2,5,4-Cl2(O2N)C6H2Me (5 g.) slurried in 15 cc. 80% H2SO4, heated to 65.degree., treated during 20 min. with 9.3 g. K2Cr2O7, the mixt. heated 1 hr. at 65.degree., dild. with an equal vol. of H2O, filtered, the ppt. treat ed in 140 cc. H2O at 60.degree. with Na2CO3 to an alk. reaction, the soln. filtered, cooled, neutralized, and the ppt. recrystd. twice from 50% EtOH gave 1.2 g. 2,5,4-Cl2(O2N)C6H2CO2H (XXIII), m. 207-10.degree.. XXIII (0.5 g.),

1 cc. SOCl2, and 1 drop pyridine refluxed 0.5 hr., the excess SOCl2 removed in vacuo, and the residue recrystd. from 5 cc. naphtha (b. 135-45.degree.) yielded 0.284 g. 2,5,4-Cl2(O2N)C6H2COCl (XXIV), m. 62-4.degree.. Crude XXIV condensed with glutamic acid in aq. alkali gave (2,5-dichloro-4-nitrobenzoyl)glutamic acid (XXV), m. 182-5.degree.; in a similar but larger run the yield of XXV was 78%. XXV reduced with a Zn-Cu couple in dil. acid, and the resulting soln. (contg. a 75% yield of amine) condensed with XIV and XII and with MeCHClCCl2CHO gave crude products which did not show interesting biol. activity. 2,6,4-Cl2(O2N)C6H2Me, prepd. in 9-17% yields by the method of Davies, (5 g.), 8 cc. 70% HNO3, and 16 cc. H2O heated 16.5 hrs. in a sealed tube at 140.degree., and the resulting crude product partially purified by repptn. from aq. NaHCO3 with acid and recrystn. from H2O gave 62-9% 2,6,4-Cl2(O2N)C6H2CO2H (XXVI), m. 175.6-6.4.degree.. XXVI heated with excess SOCl2 in the presence of a small amt. pyridine gave 2,6,4-Cl2(O2N)C6H2COCl (XXVII) which was used without further purification. XXVI (10 g.), 50 cc. SOCl2, and 20 drops pyridine refluxed 1 hr., the excess SOCl2 removed in vacuo, the residue refluxed 5 hrs. with 200 cc. MeOH, the excess MeOH distd. off, the solid residue slurried in ice-water with sufficient NaHCO3 to give an alk. reaction, and the solid filtered off and dried gave 10.4 g. Me ester of XXVI, m. 119-21.5.degree. (recrystd. from boiling MeOH, m. 121.5-3.5.degree.). Crude XXVII (0.4 g.) treated with 0.235 g. glutamic acid in aq. alkali gave (2,6-dichloro-4-nitrobenzoyl)glutamic acid, m. 215-20.degree.. A 25:75 mixt. of 2- and 4-nitroxylenes oxidized with CrO3 in glacial AcOH yielded 25% 3,4-Me(O2N)C6H3CO2H (XXVIII), m. 216-17.degree.. XXVIII (18.1 g.), 650 cc. MeOH, and 11.8 g. 100% H2SO4 refluxed 20 hrs. yielded 95% Me ester (XXIX) of XXVIII, m. 80-1.degree.. XXIX (270 g.) dissolved in 4200 cc. MeOH at 40-5.degree., the soln. cooled to 30.degree., treated under N with N2H4.H2O, the mixt. stirred at room temp. overnight under N, and the solid filtered off, washed with H2O, and dried yielded 135.2 g. 3,4-Me(O2N)C6H3CONHNH2 (XXX), m. 149-50.degree.; the mother liquors concd. and dild. with H2O gave an addnl. 96.5 g. (total yield 86%) XXX. XXX converted to the azide and condensed with glutamic acid yielded 62.8% di-Et (3-methyl-4-nitrobenzoyl)glutamate (XXXI), m. 66.5-7.4.degree.. XXXI hydrolyzed in dil. aq. NaOH, then reduced with ZnCu couple, and the soln. (contg. a 100% yield of the amino compd.) condensed with XI and XII gave 3'-methylpteroylglutamic acid (XXXII) (chem. assay 27-36%), which, purified in the usual manner, yielded XXXII.2.5H2O, .lambda.max. 255, 285, 365, .lambda.min. 236, 267, 330 m.mu.. XXXI hydrolyzed, reduced, and condensed with XIV and XII and the product purified in the usual manner gave similarly 4-amino-3'-methylpteroylglutamic acid (XXXIII), crystg. with 2 moles H2O, .lambda.max. 260, 280, 370, .lambda.min. 240, 274, 330 m.mu.. Nitromesitylenic acid (XXXIV) (35.5 g.) treated with 118 g. SOCl2 and 2-3 cc. pyridine, and the crude product recrystd. from naphtha gave 3,5,4-Me2(O2N)C6H2COCl, m. 52-3.degree., which did not condense with glutamic acid. XXXIV refluxed with MeOH and H2SO4 gave 97% Me ester (XXXV) of XXXIV, m. 107.5-109.degree.. XXXV was converted to 86% 3,5,4-Me2(O2N)C6H2CONHNH2 (XXXVI), m. 172.8-3.7.degree. (pptd. from dil. acid with NH4OH), converted by the azide method to 68% di-Et(3,5-dimethyl-4-nitrobenzoyl)glutamate (XXXVII), m. 87.5-9.0.degree. (pptd. several times from EtOH with H2O). XXXVII hydrolyzed in dil. alkali, reduced, condensed with XIV and (4-amino-3,5-dimethylbenzoyl)glutamic acid, and the product purified

in the usual manner gave 4-amino-3',5'-dimethylpteroylglutamic acid (XXXVIII), .lambda.max. 259, 370, .lambda.max. 238, 325 m.mu.. The biol. activity of the substituted pteroylglutamic acids (+ = growth activity as compared to I with an arbitrary value of 100 for half-max. inhibition of the growth of S. faecalis) was: VII +0.22, III -0.3, XIII -0.8, XXXII -1.5, VIII 0, XX -11.2, XV -80, XXXIII -160, XXXVIII -2.4.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:56:02 ON 05 SEP 2002)

L7 7899 SEA ((STREPTOCOCC? OR S)(W) PNEUMON? OR STREPTOCOC?)(5A)(TREAT? OR THERAP?)

L9 34 SEA L7(10A) ANTAGONIST?

L10 34 DUP REM L9 (0 DUPLICATES REMOVED)

L10 ANSWER 1 OF 34 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-031927 [04] WPIDS
DOC. NO. CPI: C2001-009793
TITLE: Antagonist or agonist of staphylococcal Fab I enoyl-acyl carrier protein (ACP) reductase polypeptides, useful for treating infections caused by Staphylococcus and Streptococcus species.
DERWENT CLASS: B04 D16
INVENTOR(S): DEWOLF, W E
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000070017	A2	20001123	(200104)*	EN	104
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 1180164	A2	20020220	(200221)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000070017	A2	WO 2000-US12104	20000504
EP 1180164	A2	EP 2000-935862	20000504
		WO 2000-US12104	20000504

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1180164	A2	Based on	WO 200070017

PRIORITY APPLN. INFO: US 1999-134362P 19990514
AN 2001-031927 [04] WPIDS
AB WO 200070017 A UPAB: 20010118
NOVELTY - An antagonist (A1) that inhibits, or agonist (A2) that activates, the activity of staphylococcal Fab I enoyl-acyl carrier protein (ACP) reductase (FAB I) polypeptide comprising a sequence having at least 90% identity to a sequence (S1), fully defined in

the specification, is new.

DETAILED DESCRIPTION - FAB I comprises a sequence having at least 90% identity to S1 comprising 256 amino acids fully defined in the specification, or CGCGGATCCAATCAAGTCAGGTTGAAATATCCA. Activity of FAB I is uncompetitive inhibition by Apo-ACP versus NAD (nicotinamide adenine dinucleotide) H (Ki(app)), competitive inhibition by Apo-ACP versus crotonoyl coenzyme A (CoA), induction of negative cooperativity with respect to CCA (not defined) binding, use of NADH and NADP (nicotinamide adenine dinucleotide phosphate) H as substrates by Fab I, binding of NADH and NADPH of Fab I, oxidation of NADH and NADPH by Fab I, ratio of Kmapp for NADH as compared to NADPH, use of NADH and crotonoyl CoA as substrates by Fab I in sequential kinetic mechanism, sequential binding of NADH and crotonoyl CoA by Fab I, increasing inhibition of Fab I by saturated fatty acyl CoA's of increasing chain length, feedback regulator mechanism of Fab I by saturated fatty acyl CoA's, competitive inhibition of palmitoyl CoA versus crotonoyl CoA, competitive inhibition of palmitoyl CoA versus crotonoyl CoA modulation through binding of multiple palmitoyl CoA molecules of Fab I, binding of multiple palmitoyl CoA molecules of Fab I, negative cooperativity in the binding of CCA, formation of a dimeric, tetrameric or oligomeric quaternary structure, binding of Fab I by pseudo-product inhibitors beta-NADP+ or palmitoyl CoA, or NADH binding to Fab I prior to or simultaneous with ACP binding.

ACTIVITY - Antibacterial; auditory; respiratory general; antithyroid; opthalmological; osteopathic; dermatological; nephrotropic; antidiarrheic.

No biological data is given.

MECHANISM OF ACTION - Antagonist or agonist of FAB I polypeptide.

No biological data is given.

USE - A1 and A2 are useful for treating an individual infected with bacteria such as Streptococcus or Staphylococcus, preferably Staphylococcus aureus or Streptococcus pneumoniae. A1 and A2 are useful for preventing, inhibiting and/or treating respiratory tract infections such as otitis media, bacterial trachitis, acute epiglottis, thyroiditis, empyema and lung abscess, cardiac infections such as infective endocarditis, gastrointestinal infections such as secretory diarrhea, splenic abcess and retroperitoneal abscess, central nervous system infections such as cerebral abscess, eye infections such as blepharitis, conjunctivitis, keratitis, endophthalmitis, preseptal and orbital cellulitis and darcryocystitis, kidney and urinary tract infection such as epididymitis, intrarenal and perinephric abscess and toxic shock syndrome, skin infections such as impetigo, folliculitis, cutaneous abscesses, cellulitis, wound infection, bacterial myositis, and bone and joint infections such as septic arthritis and osteomyelitis.

Dwg.0/17

L10 ANSWER 2 OF 34 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-007407 [01] WPIDS

DOC. NO. NON-CPI: N2001-005316

DOC. NO. CPI: C2001-001906

TITLE: Antagonist and agonist that activates or inhibits Staphylococcus RNaseP RNA, useful for treating S. aureus and Streptococcus pneumoniae infections such as otitis media, empyema, and keratitis.

DERWENT CLASS: B04 D16 S03
INVENTOR(S): GRESS, M J; HEGG, L A; LI, H; PARK, J J
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000068430	A1	20001116	(200101)*	EN	82

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000068430	A1	WO 2000-US12252	20000504

PRIORITY APPLN. INFO: US 1999-133069P 19990507
AN 2001-007407 [01] WPIDS
AB WO 200068430 A UPAB: 20001230
NOVELTY - An antagonist (I) that inhibits, or an agonist (II) that activates, activity of RNA transcribed from a polynucleotide which has 90% identity to a fully defined RNaseP RNA gene sequence of 400 nucleotides (S3) as given in the specification, or a polynucleotide comprising (S3), is new.

DETAILED DESCRIPTION - An antagonist (I) that inhibits, or an agonist (II) that activates, activity of RNA transcribed from a polynucleotide which has 90% identity to a fully defined RNaseP RNA gene sequence of 400 nucleotides (S3) as given in the specification, or a polynucleotide comprising (S3), is new. The compound modulates DEPC (not defined) cleavage of nucleotides 159-161, A211-213.A203, 204, or A169, 292-294(L15.2), 271 (bulged A).

The activity of the RNA which is to be activated or inhibited is Staphylococcus aureus RNaseP Km = 53 plus or minus 4 or RNase PKcat = 3.4 plus or minus 0.1 min-1 determined in a reaction in 1 multiply buffer comprising 100 mM Tris-Cl (pH 7.0), 150 mM KCl, 10 mM MgCl2, 5% PEG (polyethylene glycol), and (E) = 20 nM using cloned pre-tRNAphe as a substrate, S. aureus RNaseP RNA binding isotherm of Kd = 8 plus or minus 1 nM for RNaseP protein determined in a reaction buffer comprising 20 mM K-Hepes (pH 8.0), 0.01% NP-40, 400 mM NH4OAc, 10 mM MgCl2, 5% glycerol, S. aureus RNaseP VI cleavage of nucleotides 8-11, 16-23, 30-33, 37-54, 64-84, 96-105, 119-130, 150-156, 166-169, 181-184 or 290-294, or S. aureus RNase T2 cleavage of nucleotides 24-27, 55-60, 86-91, 106-108, 135-138 or 170-177.

INDEPENDENT CLAIMS are also included for the following:

(1) treating an individual infected with a bacteria, comprising administering an antagonist or agonist that inhibits or activates the activity of RNaseP as described above;

(2) an antagonist (III) that inhibits the activity of RNaseP polypeptide having a fully defined sequence of 117 amino acids as given in the specification; and

(3) inhibiting activity of RNaseP RNA or holoenzyme and inhibiting growth of bacteria, comprising contacting a composition containing the polypeptide or the bacteria, with an antagonist that inhibits activity of RNaseP, or RNaseP RNA or holoenzyme,

respectively.

ACTIVITY - Auditory; antiinflammatory; antibacterial; antidiarrheic; ophthalmological; immunosuppressive; dermatological; antiarthritic.

No biological data is given.

MECHANISM OF ACTION - RNaseP activity inhibitors; immune response stimulator; bacterial adherence to damaged tissues, inhibitor; gene therapy.

No biological data is given.

USE - (I), (II) or (III) is useful for treating an individual having need to inhibit or activate RNaseP RNA or holoenzyme and for treating an individual infected with a bacteria such as S. aureus and Streptococcus pneumoniae by inhibiting or activating the activity of RNaseP. It is also used for inhibiting or activating S. pneumoniae RNaseP RNA. The antagonists and agonists are useful for inhibiting and treating diseases such as, infection of the upper respiratory tract (otitis media, bacterial tracheitis, acute epiglottitis, thyroiditis), lower respiratory tract, heart, gastrointestinal system (secretory diarrhea, splenic abscess, retroperitoneal abscess), CNS, eye (blepharitis, conjunctivitis, keratitis, endophthalmitis), kidney and urinary tract (epididymitis, intrarenal and perinephric abscess), skin (impetigo, folliculitis, cutaneous abscesses, cellulitis), and bones and joints (septic arthritis, osteomyelitis). The agonist or antagonist is useful in interfering with the initial physical attraction between a pathogen and a mammalian host which is responsible for further infection. The molecules are useful for preventing adhesion of gram positive bacteria to mammalian extracellular matrix proteins on in-dwelling devices or to extracellular matrix proteins in wounds, to block RNaseP protein-mediated cell invasion by initiating phosphorylation of mammalian tyrosine kinases, to block bacterial adhesion between mammalian extracellular matrix proteins and bacterial RNaseP proteins that mediate tissue damage and/or to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or by other surgical techniques.

Dwg.0/1

L10 ANSWER 3 OF 34 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-016077 [02] WPIDS

DOC. NO. CPI: C2001-004433

TITLE: Novel 5-enolpyruvylshikimate-3-phosphate synthase protein from Streptococcus pneumoniae useful for identifying agonists and antagonists of aroA activity for treating otitis media, conjunctivitis and pneumonia.

DERWENT CLASS: B04 D16

INVENTOR(S): BROWN, J R; CHALKER, A F; DU, W; KATZ, L K; MAZZULLA, M J; PAYNE, D J; TRAINI, C M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC

COUNTRY COUNT: 27

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000068243	A1	20001116	(200102)*	EN	70

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP US
EP 1179002 A1 20020213 (200219) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000068243	A1	WO 2000-US12251	20000504
EP 1179002	A1	EP 2000-928848	20000504
		WO 2000-US12251	20000504

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1179002	A1	Based on	WO 200068243

PRIORITY APPLN. INFO: US 1999-133070P 19990507
AN 2001-016077 [02] WPIDS
AB WO 200068243 A UPAB: 20010110
NOVELTY - A polypeptide (I) comprising 70 % identity to a 427 residue amino acid sequence (S2), fully defined in the specification, and corresponding to 5-enolpyruvylshikimate-3-phosphate synthase (AroA) from Streptococcus pneumoniae, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) comprising 70 % identity to a polynucleotide encoding a polypeptide comprising (S2), or to a polynucleotide encoding the same mature polypeptide expressed by the aroA gene contained in the S. pneumoniae of the deposited strain, or comprising a sequence encoding (I), a sequence complementary to the above mentioned polynucleotides, or a sequence which comprises at least 15 sequential bases of the above mentioned polynucleotides;

(2) a vector (III) comprising (II);

(3) a host cell (IV) comprising (III);

(4) preparation of (I), comprising culturing (IV) under optimum conditions sufficient for the production of the polypeptide or its fragment;

(5) an antibody (V) against (I);

(6) identifying compounds which interact with and inhibit or activate an activity of (I), comprising:

(a) contacting a composition comprising the polypeptide with the compound to be screened under interaction conditions, the interaction being associated with a second component capable of providing detectable signal in response to the interaction of the polypeptide with the compound; and

(b) determining if the compound interacts with and activates or inhibits an activity of the polypeptide by detecting the presence or absence of a signal generated from the interaction of the compound with the polypeptide;

(7) an antagonist (VI) which inhibits the activity or expression of (I);

(8) an antagonist that inhibits, or an agonist (VII) that activates, an activity of the polypeptide which comprises 90 % identity to (S2) or a 415 residue amino acid sequence (S4), fully defined in the specification, the activity of the protein being:

(a) synthesis of p-aminobenzoate and ubiquinone;

(b) transformation of phospho(enol)pyruvate (PEP) and shikimate 3-phosphate (S3P) to 5-enolpyruvylshikimate-3-phosphate synthase (EPSP) an inorganic phosphate (Pi);

(c) transformation of EPSP and Pi to PEP and S3P;

(d) binding of

(i) AroA and PEP;

(ii) AroA to PEP-pyruvate kinase complex;

(iii) AroA to PEP-lactate dehydrogenase complex; and

(iv) AroA and S3P;

(e) competitive inhibition of the forward reaction of AroA by (i) glyphosate versus PEP (ii) EPSP versus PEP and (iii) EPSP versus S3P;

(f) competitive inhibition of the reverse reaction of AroA by S3P versus EPSP;

(g) uncompetitive inhibition of the forward reaction of AroA by glyphosate versus S3P;

(h) uncompetitive inhibition of the reverse reaction of AroA by (i) glyphosate versus EPSP and (ii) S3P versus Pi; and

(i) noncompetitive inhibition of the reverse reaction of AroA by glyphosate versus Pi;

(9) treating an individual infected with bacteria by administering a compound that is a competitive inhibitor of S3P substrate use by AroA;

(10) inhibiting an activity of AroA, and a conversion of acetyl-CoA to a product or conversion of malonyl-ACP to product, comprising contacting a composition comprising bacteria with a compound that inhibits the activity for a sufficient time to cause killing or slowing growth of the bacteria; and

(11) inhibiting growth of bacteria.

ACTIVITY - Antibacterial; antiinflammatory; ophthalmological. No biological data is given.

MECHANISM OF ACTION - AroA activity inhibitors; immune response stimulator; bacterial adherence to damaged tissues, inhibitor; gene therapy.

USE - (I) is useful for treating an individual in need of AroA polypeptide. (I) and (II) are useful as diagnostic reagents for diagnosing a disease related to their expression or activity in an individual which comprises determining a nucleic acid sequence encoding the polypeptide and/or analyzing for the presence or amount of the polypeptide in a sample derived from the individual. (I) is useful for inducing an immunological response in a mammal comprising inoculating the polypeptide, its fragment or variant, or delivering a nucleic acid vector to direct expression of the polypeptide in vivo, in order to induce an immunological response to produce antibody and/or T-cell immune response to protect the animal from the disease. (VI) is useful for inhibiting the activity of the AroA polypeptide and for inhibiting the growth of a bacterial composition and also for inhibiting AroA polypeptide. (VII) is used to inhibit or activate AroA polypeptide and for treating individuals infected with bacteria of the genus Staphylococcus, S. aureus, a member of Streptococcus genus such as Streptococcus pneumoniae. (All claimed). (I), its antagonists and agonists are useful for treating otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema and endocarditis and most particularly meningitis. (II) is useful for gene therapy techniques. The polynucleotides may be used as hybridization probes to isolate full length cDNAs and genomic clones encoding AroA and to isolate cDNA and genomic clones

of other genes that have a high sequence similarity to the AroA gene. (I) and (II) are also useful as research reagents and materials for discovery of treatments of and diagnostics for human diseases. The DNA sequences may be used in the discovery of antibacterial compounds and to construct antisense sequences to control the expression of the coding sequence of interest. The encoded protein is useful as a target for screening antibacterial drugs. The polynucleotides or its fragments which encode non-variable regions of the bacteria cell surface proteins in DNA constructs used in the genetic immunization experiments in animal models of Streptococcus pneumoniae infections are useful in identifying protein epitopes able to provoke a prophylactic or therapeutic immune response. The polypeptides are used as antigens for vaccination of a host to produce specific antibodies which protect against invasion of bacteria by blocking adherence of bacteria to damaged tissues such as wounds in the skin or connective tissue caused by mechanical, chemical or thermal damage, or by implantation of indwelling devices, or wounds in the mucous membranes. The novel molecules are useful for preventing adhesion of gram positive and/or gram negative bacteria, to mammalian extracellular matrix proteins on in-dwelling devices or to extracellular matrix proteins in wounds, to block AroA protein-mediated cell invasion by initiating phosphorylation of mammalian tyrosine kinases, to block bacterial adhesion between mammalian extracellular matrix proteins and bacterial AroA proteins that mediate tissue damage and/or to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or by other surgical techniques.
Dwg.0/6

L10 ANSWER 4 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-016050 [02] WPIDS
DOC. NO. CPI: C2001-004422
TITLE: **Streptococcus** FabH **antagonists**, useful for **treatment** of bacterial infection.
DERWENT CLASS: B04 D16
INVENTOR(S): KONSTANTINIDIS, A K; LONSDALE, J T; VAN ALLER, G S
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000067780	A1	20001116	(200102)*	EN	48
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 1178820	A1	20020213	(200219)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000067780	A1	WO 2000-US12250	20000504
EP 1178820	A1	EP 2000-928847	20000504
		WO 2000-US12250	20000504

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1178820	A1 Based on	WO 200067780

PRIORITY APPLN. INFO: US 1999-132714P 19990506
AN 2001-016050 [02] WPIDS
AB WO 200067780 A UPAB: 20010110
NOVELTY - An antagonist (ANT) that inhibits the activity or expression of a polypeptide (PEP) comprising an amino acid sequence with at least 90% identity to a 313 or 324 amino acid sequence given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) methods for treatment of an individual infected by a bacteria or in need of inhibited FabH activity, comprising administering ANT which inhibits the activity or expression of PEP or that inhibits either the conversion of acetyl-CoA to a product by FabH action or the conversion of malonyl-acyl carrier protein (ACP) to a product by action of FabH;

(2) a method for inhibiting FabH comprising contacting an antagonist that inhibits conversion of acetyl-CoA or malonyl-ACP to products to the polypeptide; and

(3) inhibiting conversion of acetyl-CoA or malonyl-ACP products, comprising contacting a bacteria with a compound that inhibits such conversion.

ACTIVITY - Antibacterial.
No biological data given.
MECHANISM OF ACTION - FabH antagonist; Vaccine.
USE - The antagonist is useful for treatment of an individual in need of inhibited FabH polypeptide activity and expression. The antagonist can be used to treat an individual infected with a bacteria, such as Staphylococcus sp., S. aureus, Streptococcus sp. and S. pneumoniae. The antagonist inhibits conversion of acetyl-CoA or malonyl-ACP to product. The antagonist can be used to inhibit FabH and to inhibit growth of a bacteria (claimed).
Dwg.0/0

L10 ANSWER 5 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-515100 [46] WPIDS
DOC. NO. CPI: C2000-153745
TITLE: Isolated nadE polypeptide useful for screening for agonists and **antagonists** useful for **treatment** of infections, is derived from **Streptococcus pneumoniae.**
DERWENT CLASS: B04 D16
INVENTOR(S): BISWAS, S; BURNHAM, M K R; CHALKER, A F; INGRAHAM, K A; TRAINI, C M; WARREN, P V; ZALACAIN, M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000049042	A1	20000824	(200046)*	EN	43

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP
US 6251631 B1 20010626 (200138)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000049042	A1	WO 2000-US3847	20000215
US 6251631	B1	US 1999-250677	19990216

PRIORITY APPLN. INFO: US 1999-250677 19990216
AN 2000-515100 [46] WPIDS
AB WO 200049042 A UPAB: 20000921
NOVELTY - An isolated mature nadE polypeptide derived from Streptococcus pneumoniae (I) comprising, or having at least 95% identity to, the fully defined 274 amino acid sequence and encoded by a fully defined 825 base pair sequence, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) encoding (I), comprising, or having at least 95% identity to, the fully defined 825 base pair sequence that is at least 30 nucleotides in length, or its antisense sequence;

(2) preparation of (I);

(3) a host cell (III) or a membrane expressing (I);

(4) preparation of (III) comprising an expression system or a membrane expressing (I);

(5) an antibody (IV) immunospecific for (I); and

(6) an agonist or antagonist to (I).

USE - (I) may be used to screen for its agonists and antagonists by contacting (I) with the candidate compound and detecting any alteration in activity of (I) or in a label attached to the candidate. Alternatively, the effect of a candidate agonist or antagonist on the production of mRNA encoding (I) may be detected using an ELISA assay (both claimed). Diseases or conditions arising from altered expression or activity of (I) may be diagnosed by detecting (I) in a sample from a patient or detecting a mutation in (II) in the genome of a patient (claimed). These diseases or conditions include bacterial infections, especially Streptococcus pneumoniae and Helicobacter pylori infections that cause stomach cancer, ulcers and gastritis. Antagonists of (I) may be administered to patients suffering from the above diseases related to increased expression or activity of (I). Agonists may be similarly used in cases of diseases or conditions related to decreased expression or activity of (I). Antisense sequences to (II) may also treat conditions related to increased expression of (I). Antibodies against (I) may be used to isolate or identify clones expressing (I) or to purify (I) by affinity chromatography.
Dwg.0/0

L10 ANSWER 6 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-558288 [51] WPIDS
DOC. NO. CPI: C2000-166260
TITLE: Novel Streptococcus pneumoniae yybQ polypeptide and polynucleotide sequences, used to treat and diagnose microbial infections, and to identify agonists, antagonists and antibiotic compounds.

DERWENT CLASS: B04 D16
INVENTOR(S): BISWAS, S; BURNHAM, M K R; CHALKER, A F; INGRAHAM, K A; SO, C Y; TRAINI, C M; ZALACAIN, M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000049033	A1	20000824	(200051)*	EN	39

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000049033	A1	WO 2000-US3774	20000215

PRIORITY APPLN. INFO: US 1999-251639 19990217
AN 2000-558288 [51] WPIDS
AB WO 200049033 A UPAB: 20001016
NOVELTY - A polypeptide (I) comprising at least 95 % identity to a 311 residue Streptococcus pneumoniae yybQ polypeptide sequence, fully defined in the specification, or which comprises or is the 311 residue sequence, or is encoded by a 936 nucleotide sequence, fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide (II) selected from:

(a) a polynucleotide encoding (I);

(b) a polynucleotide having at least 95 % identity to a 936 nucleotide sequence, fully defined in the specification;

(c) a polynucleotide comprising the 936 nucleotide sequence;

(d) an at least 30 nucleotide sequence obtained by screening a library under stringent hybridization conditions with a probe having a fragment of at least 30 nucleotides of the 936 nucleotide sequence;

(e) a polynucleotide encoding mature Streptococcus pneumoniae yybQ polypeptide; and

(f) a polynucleotide complementary to any of (a)-(e);

(2) diagnosing or prognosing a disease or susceptibility to it, related to expression or activity of (I), comprising determining the presence or absence of a mutation in the nucleotide sequence encoding (I) in the individual, or analyzing for the presence or amount of (I) expression in a sample derived from the individual;

(3) producing (I), using a host cell;

(4) producing a host cell comprising an expression system or membrane expressing (I), comprising transforming or transfecting the cell with an expression system comprising a polynucleotide capable of producing (I) when cultured under expression conditions in a host cell;

(5) a host cell or a membrane expressing (I);

(6) an antibody immunospecific for (I);

(7) screening to identify compounds that agonize or inhibit (I) function, comprising:

(a) measuring binding of a candidate compound to (I) or a

fusion protein of it, using a direct or indirect label;

(b) measuring binding of a candidate compound to (I) or a fusion protein of it, in the presence of a labeled competitor;

(c) testing if the candidate compound results in a signal generated by activation or inhibition of (I);

(d) mixing a candidate compound with a solution comprising (I) to form a mixture, measuring activity of (I) in the mixture and comparing it to a standard; or

(e) detecting the effect of a candidate compound on the production of mRNA encoding (I) and (I) in cells, using e.g. enzyme linked immunosorbent assay (ELISA); and

(8) an agonist or antagonist of (I).

ACTIVITY - Auditory; antibacterial; antiinflammatory.

MECHANISM OF ACTION - (I) antagonist; (I) expression inhibitor; (I) ligand, substrate or receptor competitor. No biological data is given.

USE - Agonists of (I) can be used to treat individuals needing enhanced activity or expression of, or immunological response to (I). Antagonists of (I), (I) expression inhibitors, (I) ligand, substrate or receptor competitors and a polypeptide which induces an immune response to (I) can be administered to treat individuals needing to inhibit activity or expression of (I). The methods can be used to diagnose and prognose diseases associated with expression or activity of (I), and to identify antibiotics which agonize or inhibit the function of (I). All claimed. (I) and (II) can be used to treat microbial infections. (I) and (II) can also be used to identify agonists and antagonists which can be used to treat microbial infections and conditions related to them, such as otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema, and endocarditis.

Dwg.0/0

L10 ANSWER 7 OF 34 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-482971 [42] WPIDS

DOC. NO. CPI: C2000-145403

TITLE: FabG polypeptide, isolated from **Streptococcus pneumoniae**, is used to **treat** microbial diseases, identify agonists and **antagonists** for treating microbial infections and to detect diseases associated with microbial infections.

DERWENT CLASS: B04 D16

INVENTOR(S): CHALKER, A F; DEBOUCK, C; HOLMES, D J; INGRAHAM, K A; JAWORSKI, D D; KOSMATKA, A L; MCDEVITT, D; MOONEY, J; PEARSON, S C; SO, C Y; WALLIS, N G; WANG, M; WARREN, R L; ZHONG, Y Y

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 21

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044885	A1	20000803	(200042)*	EN	40
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL OA PT SE					
W: JP					
US 6346395	B1	20020212	(200219)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000044885	A1	WO 2000-US1131	20000119
US 6346395	B1	US 1999-239052	19990127

PRIORITY APPLN. INFO: US 1999-239052 19990127
AN 2000-482971 [42] WPIDS
AB WO 200044885 A UPAB: 20000905
NOVELTY - An isolated polypeptide (P1), FabG, from Streptococcus pneumoniae, is new.

DETAILED DESCRIPTION - Isolated polypeptide, FabG from S. pneumoniae, comprises:

(1) an isolated polypeptide comprising an amino acid (aa) sequence with at least 95% identity to aa sequence (I) of 243 aa from S. pneumoniae given in the specification, over the entire length of (I);

(2) an isolated polypeptide comprising (I);

(3) an isolated polypeptide that is (I); or

(4) a polypeptide encoded by a recombinant polynucleotide comprising polynucleotide sequence (II) of 732 base pairs from S. pneumoniae, given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide that is:

(a) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide with at least 95% identity to aa sequence (I) over the entire length of (I);

(b) an isolated polynucleotide comprising a polynucleotide sequence with at least 95% identity over its entire length to a polynucleotide sequence encoding (I);

(c) an isolated polynucleotide comprising a nucleotide sequence with at least 95% identity to (II), over the entire length of (II);

(d) an isolated polynucleotide comprising a nucleotide sequence encoding (I);

(e) an isolated polynucleotide that is (II);

(f) an isolated polynucleotide at least 30 nucleotides long obtained by screening an appropriate library under stringent hybridization conditions with a probe having the sequence of (II), or a fragment of (II) at least 30 nucleotides long;

(g) an isolated polynucleotide encoding a mature polypeptide expressed by the FabG gene comprised in the S. pneumoniae; and

(h) a polynucleotide sequence complementary to the isolated polynucleotide of one of (a) - (g);

(2) a method for treating an individual:

(a) in need of enhanced activity or expression of or immunological response to (P1) comprising administering to the individual an antagonist to (P1); or

(b) in need of inhibition of activity or expression of (P1) comprising administering an antagonist to (P1), a nucleic acid molecule that inhibits expression of a polynucleotide sequence encoding (P1), a polypeptide that competes with (P1) for its ligand, substrate or receptor or administering a polypeptide that induces an immunological response to (P1) in the individual;

(3) a process for diagnosing or prognosing a disease or susceptibility to a disease in an individual related to expression or activity of (P1) in an individual comprising determining the presence or absence of a mutation in the nucleotide sequence

encoding (P1) or analyzing for the presence or amount of expression in a sample derived from the individual;

(4) a process for producing (P1) comprising culturing a host cell under conditions for production of (P1);

(5) a process for producing a host cell comprising an expression system or a membrane expressing (P1) comprising transforming or transfecting a cell with an expression system comprising a polynucleotide capable of producing (P1) when the expression system is present in a compatible host cell so that under suitable culture conditions the host cell produces (P1);

(6) a host cell or membrane expressing (P1);

(7) an antibody immunospecific for (P1);

(8) a method for screening to identify compounds that antagonize or inhibit the function of (P1) comprising:

(a) measuring the binding of a candidate compound to (P1) (or to the cells or membranes bearing (P1)) or a fusion protein of (P1) using a label directly or indirectly associated with the candidate compound;

(b) measuring the binding of a candidate compound to (P1) (or to the cells or membranes bearing (P1)) or a fusion protein of (P1) in the presence of a labeled competitor;

(c) testing whether the candidate compound results in a signal generated by activation or inhibition of (P1) using detection systems appropriate to the cells or cell membranes bearing (P1);

(d) mixing a candidate compound with a solution comprising (P1) to form a mixture, measuring activity of (P1) in the mixture and comparing the activity of the mixture to a standard; or

(e) detecting the effect of a candidate compound on the production of mRNA encoding (P1) and on (P1) in cells, e.g. by using an enzyme linked immunosorbent assay (ELISA); and

(9) an agonist or antagonist to (P1).

ACTIVITY - Antibacterial; cytostatic; antiulcer.

No biological data given.

MECHANISM OF ACTION - None given.

USE - (P1) and the polynucleotides encoding (P1) are used to treat microbial diseases, identify antagonists and agonists which can then be used to treat microbial infections and conditions associated with the infections, and to detect diseases associated with microbial infection. The compounds are used to interfere with the initial physical interaction between a pathogen or pathogens and a eukaryotic, preferably mammalian, host, in particular to prevent the adhesion of bacteria to mammalian extracellular proteins in wounds, prevent adhesion between mammalian extracellular proteins and bacterial FabG proteins which mediate tissue damage and/or to block normal progression of pathogenesis in infections mediated by implantation of in-dwelling devices or other surgical techniques. In particular (P1), its polynucleotides, antagonists and agonists are used to treat Helicobacter pylori infection to decrease H. pylori-induced cancers and to prevent, inhibit and/or cure gastric ulcers and gastritis.

Dwg.0/0

L10 ANSWER 8 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-491237 [43] WPIDS
DOC. NO. CPI: C2000-147692
TITLE: New Streptococcus pneumoniae MurA polynucleotide and MurA polypeptide, useful as diagnostic reagents in the diagnosis of S. pneumoniae infections.

DERWENT CLASS: B04 D16
INVENTOR(S): HUANG, J; JIANG, X; PAYNE, D; VAN HORN, S; WALLIS, N G
PATENT ASSIGNEE(S): (HUAN-I) HUANG J; (JIAN-I) JIANG X; (PAYN-I) PAYNE D; (VHOR-I) VAN HORN S; (WALL-I) WALLIS N G; (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044779	A1	20000803	(200043)*	EN	36
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE W: JP					
US 6346396	B1	20020212	(200219)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000044779	A1	WO 2000-US1307	20000120
US 6346396	B1	US 1999-240936	19990129

PRIORITY APPLN. INFO: US 1999-240936 19990129
AN 2000-491237 [43] WPIDS
AB WO 200044779 A UPAB: 20000907
NOVELTY - Streptococcus pneumoniae MurA polynucleotide (1260 nucleotide sequence (I)) and MurA polypeptide (419 amino acid sequence (II)), are new. Both sequences are defined in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (P1) selected from:

(a) an isolated polypeptide comprising an amino acid having at least 95 % identity to (II) over its entire length;

(b) an isolated polypeptide comprising the amino acid sequence of (II);

(c) an isolated polypeptide that is (II); or

(d) a polypeptide that is encoded by a recombinant polynucleotide comprising the sequence of (I);

(2) an isolated polynucleotide (N1) selected from:

(a) an isolated polynucleotide comprising a sequence encoding a polypeptide that has at least 95 % identity to the sequence of (II) over the entire length;

(b) an isolated polynucleotide comprising a sequence that has at least 95 % identity over its entire length to a sequence encoding (II);

(c) an isolated polynucleotide comprising a nucleotide sequence that has at least 95% identity to the sequence of (I) over its entire length;

(d) an isolated polynucleotide comprising a nucleotide sequence encoding (II);

(e) an isolated polynucleotide that is (I);

(f) an isolated polynucleotide, of at least 30 nucleotides in length obtainable by screening an appropriate library under stringent hybridization conditions with a probe, 30 nucleotides in length, having the sequence of (I) or its fragment;

(g) an isolated polynucleotide encoding a mature polypeptide expressed by the MurA gene of Streptococcus pneumoniae; or

(h) a polynucleotide sequence complementary to the isolated polynucleotides of (a) to (g);

(3) a method for the treatment of an individual:

(a) in need of enhanced activity or expression of or immunological response to P1, comprising administering an effective amount of an antagonist to the polypeptide; or

(b) having need to inhibit activity or expression of P1 comprising:

(a) administering an effective amount of an antagonist to the polypeptide;

(b) administering a nucleic acid molecule that inhibits the expression of a polynucleotide sequence encoding the polypeptide;

(c) administering an effective amount of a polypeptide that competes with P1 for its ligand, substrate, or receptor; or

(d) administering a polypeptide that induces an immunological response to P1;

(4) a process for diagnosing or prognosing a disease or a susceptibility to a disease related to expression or activity of P1 in an individual, comprising:

(a) determining the presence or absence of a mutation in the nucleotide sequence encoding the polypeptide; or

(b) analyzing for the presence or amount of the polypeptide expression in a sample derived from the individual;

(5) a process for producing a polypeptide, comprising culturing a host cell under conditions sufficient for the production of the polypeptide, where the polypeptide is P1;

(6) a process for producing a host cell containing an expression system or its membrane expressing P1, comprising transforming or transfecting the cell with an expression system comprising a polynucleotide encoding P1;

(7) a host cell or a membrane expressing P1;

(8) an antibody immunospecific for P1;

(9) a method for screening to identify compounds that agonize or that inhibit the function of P1, comprising a method selected from:

(a) measuring the binding of a candidate compound to the polypeptide (or to the cells or membranes bearing the polypeptide) or its fusion protein by means of a label directly or indirectly associated with the candidate compound;

(b) measuring the binding of a candidate compound to the polypeptide (or to the cells or membranes bearing the polypeptide) or its fusion protein in the presence of a labeled competitor;

(c) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells or cell membranes bearing the polypeptide;

(d) mixing a candidate compound with a solution comprising P1, to form a mixture, measuring activity of the polypeptide in the mixture, and comparing the activity of the mixture to a standard; or

(e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in cells, using for instance, an Enzyme linked immunoabsorbant assay (ELISA) assay; and

(10) an agonist or antagonist to P1.

ACTIVITY - Antibacterial; antiinflammatory; antiulcer.

No biological data given.

MECHANISM OF ACTION - MurA antagonist and agonist.

USE - The MurA polynucleotide and polypeptide are useful as diagnostic reagents in the diagnosis of bacterial infections, preferably S. pneumoniae infections.

The agonists and antagonists of the MurA polypeptide are useful in the treatment of Helicobacter pylori infection, gastric ulcers and gastritis.

Dwg.0/0

L10 ANSWER 9 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-387560 [33] WPIDS
DOC. NO. NON-CPI: N2000-290184
DOC. NO. CPI: C2000-117586
TITLE: New DnaB polypeptide from Streptococcus pneumoniae, useful, e.g. in vaccines, for diagnosis of infections, and for identifying antibacterial agents.
DERWENT CLASS: B04 D16 T01
INVENTOR(S): CHALKER, A F; HOLMES, D J; INGRAHAM, K A; JAWORSKI, D D; LENOX, A L; MAY, E W; MAZZULLA, M J; RAY, J; WANG, M; WARREN, R L; LENNOX, A L; MAZZULLA, M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000028820	A1	20000525	(200033)*	EN	59
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP					
US 6204014	B1	20010320	(200118)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000028820	A1	WO 1999-US26893	19991111
US 6204014	B1	US 1998-191879	19981113

PRIORITY APPLN. INFO: US 1998-191879 19981113
AN 2000-387560 [33] WPIDS
AB WO 200028820 A UPAB: 20000712
NOVELTY - Isolated DnaB polypeptide (I) that is at least 70% identical with a 450 residue amino acid sequence, fully defined in the specification, over the entire length of it, comprises, or is, the 450 residue sequence, or is encoded by a recombinant polynucleotide comprising a 1953 base pair sequence, fully defined in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) polynucleotide (II) that

(a) encodes the sequence, at least 70% identical to the 450 residue sequence;

(b) is at least 70% identical with a sequence encoding the 450 residue sequence;

(c) is at least 70% identical with the 1953 base pair sequence over the entire 301-1651 nucleotide (nt) segment of it;

(d) encodes the 450 residue sequence;
(e) is the 301-1651 nt segment of the 1953 base pair sequence;
(f) is isolated by screening a library, under stringent conditions, with the 1953 base pair sequence, or a fragment of it;
(g) encodes a mature polypeptide expressed by the DnaB gene of Streptococcus pneumoniae; or
(h) is a complement of (a)-(g);
(2) antibody (Ab) immunospecific for (I);
(3) diagnosis or prognosis of disease, or susceptibility, related to expression or activity of (I), comprising determining the presence or absence of a mutation in the nucleotide sequence encoding the polypeptide in the genome of the individual, and analyzing for the presence or amount of the polypeptide expression in a sample derived from the individual;
(4) screening methods for identifying compounds (A) that activate or inhibit function of (I), comprising:
(a) measuring the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide or a fusion protein of it, using a label directly or indirectly associated with the candidate compound;
(b) measuring the binding of a candidate compound to the polypeptide or to the cells or membranes bearing the polypeptide or a fusion protein of it, in the presence of a labeled competitor;
(c) testing if the candidate compound results in a signal generated by activation or inhibition of the polypeptide;
(d) mixing a candidate compound with a solution containing (I), measuring the activity of the polypeptide, and comparing it to a standard;
(e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide, and the polypeptide in cells, using e.g. enzyme linked immunosorbant assay (ELISA); or
(f) contacting a composition comprising the polypeptide with the compound to be screened to assess the interaction, the interaction being associated with a second component capable of providing a detectable signal in response to the interaction of the polypeptide and compound, and determining if interaction occurs;
(5) agonists and antagonists of the expression or activity of (I);
(6) expression system comprising (II), present in a host cell;
(7) host cell, or its membrane, that contains the system of (6) and expresses (I);
(8) production of (I) by culturing cells of (7);
(9) production of cells of (7), or its membranes, by transformation or transfection;
(10) computer-readable medium containing at least the 450 residue sequence and/or the 1953 base pair sequence;
(11) computer-based method of homology identification, based on the 1953 base pair sequence;
(12) computer-based method of polynucleotide assembly based on identification of an overlap between the 1953 base pair sequence, and a second nucleic acid sequence; and
(13) polynucleotides of formula (IIa) X-(R1)m-R2-(R3)m-Y (IIa)

X and Y = hydrogen, metal, modified nucleotide or together form a covalent bond;
each R1 and R3 = optionally modified nucleotide;
m and n = 0-3000;
R2 = optionally modified 1953 base pair sequence.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Inhibition of DnaB, probably a replicative helicase, which is essential for growth and/or survival of S. pneumoniae.

USE - The 450 residue polypeptide, the product of the DnaB gene of Streptococcus pneumoniae, is used to screen for specific agonists and antagonists, potential therapeutic agents, to raise specific antibodies (Ab), in vaccines, and in rational drug design. Ab are useful as diagnostic immunoassay reagents and as therapeutic antagonists. Nucleic acids (II) that encode (I), or fragments, are used for recombinant production of (I), and as probes and primers to isolate homologous full-length or genomic clones, for diagnosis, prognosis, staging and typing infections, including detection of genomic mutations, and for chromosome identification or mapping. (II) can also be used in genetic immunization, and as antisense inhibitors. The therapeutic agents have bacteriostatic/bactericidal activity and are used to treat or prevent infections, especially those caused by S. pneumoniae, but also Helicobacter pylori infections and associated disorders, also for treatment of in-dwelling devices and wounds to prevent bacterial adhesion.
Dwg.0/0

L10 ANSWER 10 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-591100 [50] WPIDS
DOC. NO. NON-CPI: N1999-436014
DOC. NO. CPI: C1999-172586
TITLE: New isolated Streptococcus polypeptides, used to develop products for treating, e.g. streptococcal infections, microbial infections in plants and animals and cancers and as preservatives.
DERWENT CLASS: B04 C03 D13 D16 D22 S03
INVENTOR(S): BAST, D; BETSCHEL, S; BORGIA, S; DE AZAVEDO, J; LOW, D
PATENT ASSIGNEE(S): (MOUN) MOUNT SINAI HOSPITAL
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9949049	A1	19990930	(199950)*	EN	98
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9928232	A	19991018	(200009)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9949049	A1	WO 1999-CA240	19990318
AU 9928232	A	AU 1999-28232	19990318

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9928232 A Based on WO 9949049

PRIORITY APPLN. INFO: US 1998-78713P 19980320
AN 1999-591100 [50] WPIDS
AB WO 9949049 A UPAB: 19991201
NOVELTY - Isolated Streptococcus SAG-A polypeptides associated with streptolysin S activity are new.

DETAILED DESCRIPTION - (A) A novel isolated nucleic acid (NA) molecule (NAM) comprises:

(a) NA sequence encoding a polypeptide having sequence identity to an amino acid sequence of sequence (II) (MLKFTSNILATSVAETTQVAPGGCCCCCTTCCFSIATGSGNSQGGSGSYTPGK), (IV) (MLKFTSNILATSVAETTQVAPGG) or (VI) (CCCCCTTCCFSIATGSGNSQGGSGSYTPGK);

(b) NA sequence having at least 95% identity to a NAM encoding a polypeptide comprising an amino acid sequence (II), (IV) or (VI);

(c) NAM encoding a polypeptide comprising an amino acid sequence (II), (IV) or (VI);

(d) NA sequence complementary to (a), (b) or (c);

(e) NA sequence differing from any of (a), (b) or (c), in codon sequences due to the degeneracy of the genetic code;

(f) NA sequence comprising at least 5 nucleotides capable of hybridizing to a NA sequence (I), (III), or (V), (390, 70 or 140 nucleotides in length respectively) or to degenerate forms;

(g) NA sequence encoding a truncation, an analog, an allelic or species variation of a polypeptide comprising an amino acid sequence (II), (IV) or (VI); or

(h) fragment, or allelic or species variation of (a), (b) or (c).

INDEPENDENT CLAIMS are also included for the following:

(1) isolated NAM which comprises:

(a) NA sequence having sequence identity with an NA sequence (I), (III), or (V);

(b) NA sequences complementary to (a), preferably complementary to the full NA sequence (I), (III), or (V);

(c) NA sequences differing from any of the NA sequences as in (a) or (b) in codon sequences due to the degeneracy of the genetic code; or

(d) fragment, or allelic or species variation of (a), (b) or (c);

(2) isolated NAM comprising a nucleotide sequence (NS) selected from a group having 65%, 75%, 85%, 95% and 98% homology to the NS of sequence (I), (II), or (V);

(3) isolated NAM which hybridizes to a NAM as in (A) under stringent hybridization conditions;

(4) isolated NAM comprising a sequence selected from 8-10 nucleotides of the NAM as in (A) or (1)-(3) and 26-50 nucleotides of an NAM as in (A) or (1)-(3);

(5) isolated NAM comprising a DNA sequence obtained by screening an appropriate library containing the complete gene encoding an amino acid sequence (II) under stringent hybridization conditions with a probe having a NA sequence encoding an amino acid sequence (II) or a fragment, which fragment retains binding and/or biological activity and isolating the DNA sequence;

(6) expression vector comprising an NAM as in (A) or (1)-(5);

(7) isolated peptide produced from an NAM as in (A) or (1)-(5);

(8) isolated peptide produced from an expression vector as in (6);

(9) isolated peptide comprising an amino acid sequence (II), (IV) or (VI);

(10) isolated peptide comprising an amino acid sequence selected from a group having 65%, 75%, 85%, 95% and 98% homology to a peptide of sequence (II), (IV) or (VI);

(11) isolated peptide comprising at least 5 amino acids of a peptide as in (7)-(10);

(12) antibody directed against a peptide as in (7)-(10);

(13) cell comprising an expression vector as in (6); and

(14) chimeric toxin comprising a SAG-A polypeptide having cytolytic activity operatively linked to a targeting agent.

ACTIVITY - Antibacterial; Antifungal; Virucide; Protozoacide; Cytostatic.

USE - The products can be used to identify SagA agonists or antagonists, preferably bacteriostatic or bactericidal agonists and antagonists. Inhibitors or antagonists can be used for treating disorders including diseases caused by streptococcal infections such as endocarditis, cellulitis, brain abscesses, glomerulonephritis, pneumonia, meningitis, osteomyelitis, pharygitis, rheumatic fever, pneumonia, strep throat, scarlet fever, impetigom necrotizing fasciitis, rheumatic carditis, or toxic shock. The SAG-A peptides may be useful in both the pharmaceutical and food industries. They may exhibit antibacterial activity against a wide variety of gram-negative and gram-positive bacteria and may be used as a food preservative, an antibacterial agent for medical use, a preservative for construction materials and/or paints, an antibacterial agent for horticultural use, a preservative for livestock feed, a preservative for fish feed, and as an antibacterial agent in a wide variety of fields. They can be used to lyse microbial and eukaryotic cells including gram-positive and gram-negative prokaryotic microorganisms (e.g. bacteria, fungi, viruses, or protozoans), neoplastic cells including lymphomas, leukemias, or carcinomas, or eukaryotic cells infected with an intracellular pathogenic microorganism. The cytooolytic polypeptides may be used to treat plants and animals against microbial infections, including bacterial, yeast, fungal, viral and protozoan infections and they may be used in the treatment of cancer. They may function synergistically with conventional therapeutic agents such as antibiotics and anticancer treatments, and they may be used as adjuvants. They may also be used to selectively lyse cells using a chimeric toxin comprising a cytolytic polypeptide operatively linked to a targeting agent. The products can also be used for detection and diagnosis and in vaccines for preventing infections.

Dwg.0/7

L10 ANSWER 11 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-469316 [39] WPIDS
CROSS REFERENCE: 1997-503039 [46]; 1997-503106 [46]
DOC. NO. CPI: C1999-137758
TITLE: New human cystatin F polypeptides and polynucleotides used to treat infection, inflammation, and for protection and remodeling of the eye.
DERWENT CLASS: B04 D16
INVENTOR(S): GENTZ, R L; LI, H; NI, J; YU, G
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9938882	A1	19990805	(199939)*	EN	99
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9926535	A	19990816	(200002)		
EP 1051428	A1	20001115	(200059)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002501739	W	20020122	(200211)		108

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9938882	A1	WO 1999-US1698	19990128
AU 9926535	A	AU 1999-26535	19990128
EP 1051428	A1	EP 1999-906686	19990128
		WO 1999-US1698	19990128
JP 2002501739	W	WO 1999-US1698	19990128
		JP 2000-529349	19990128

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9926535	A	Based on	WO 9938882
EP 1051428	A1	Based on	WO 9938882
JP 2002501739	W	Based on	WO 9938882

PRIORITY APPLN. INFO: US 1998-19485 19980129
AN 1999-469316 [39] WPIDS
CR 1997-503039 [46]; 1997-503106 [46]
AB WO 9938882 A UPAB: 20020215
NOVELTY - A member of the cystatin family, cystatin F, is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I) having at least 70% identity to a member selected from:

(a) a polynucleotide encoding a polypeptide comprising either the 145 amino acid sequence given in the specification or residues 19-145 of this sequence;

(b) a polynucleotide which is complementary to (a); and

(c) a polynucleotide comprising at least 15 bases of the 633 nucleotide sequence given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide having at least 70% identity to a member selected from:

(a) a polynucleotide encoding a mature polypeptide having the amino acid sequence expressed by the human cDNA contained in ATCC deposit No. 97463;

(b) a polynucleotide which is complementary to (a); and

(c) a polynucleotide comprising at least 15 bases of the polynucleotide of (a) or (b);

(2) a polynucleotide comprising the 633 nucleotide sequence given in the specification, or bases 112-633 of this sequence;

(3) a vector comprising (I);
(4) a host cell comprising (3);
(5) a process for producing a polypeptide, comprising expressing the protein from (4);
(6) a process for producing a cell which expresses a polypeptide, comprising genetically engineering the cell with (3);
(7) a polypeptide selected from:
(a) a polypeptide having the 145 amino acid sequence given in the specification, or residues 19-145 of this sequence;
(b) a polypeptide which is at least 70% identical to the polypeptide of (a).
(8) a polypeptide comprising the 145 amino acid sequence given in the specification, or residues 19-145 of this sequence;
(9) a compound which inhibits the activation of (7);
(10) a polypeptide which activates (7);
(11) a method for the treatment of a patient having need of cystatin F, comprising administering a therapeutically effective amount of (7), optionally by providing the patient with a DNA encoding the polypeptide and expressing it in vivo;
(12) a method for the treatment of a patient having need to inhibit cystatin F, comprising administering a therapeutically effective amount of (9);
(13) a process for diagnosing a disease or susceptibility to a disease related to under-expression of (7), comprising determining a mutation in a nucleic acid encoding the polypeptide;
(14) a diagnostic process, comprising analyzing for the presence of (7) in a sample derived from a host; and
(15) a method for identifying compounds which bind to and inhibit activation of (7), comprising contacting a cell expressing on its surface a receptor for the polypeptide, the receptor being associated with a second component capable of providing a detectable signal in response to the binding of a compound to the receptor, with an analytically detectable cystatin F polypeptide and a compound under conditions to permit binding to the receptor; and determining whether the compound binds to and inhibits the receptor by detecting the absence of a signal generated from the interaction of the Cystatin F with the receptor.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The cystatin F polynucleotides are useful as a source of primers and probes, and may be used to detect complementary nucleotides such as, e.g. a diagnostic reagent. Detection of mutations of the cystatin F gene associated with a dysfunction also provides a diagnostic tool that can add to or define a diagnosis of a disease or susceptibility to a disease which results from under or over expression of cystatin F, such as neoplasia and HCCAA. The sequences of the invention are also valuable for chromosome identification and mapping. The polypeptide sequence can also be used in diagnostic assays and to produce antibodies.

Human cystatin F can also be used to block the growth of group A streptococci and replication of the herpes simplex virus and human coronaviruses, to prevent local and systemic inflammation and to modify inflammatory and necrobiotic processes in heart tissue. Cystatin F may also be used to prevent HCCAA caused by mutated cystatin F, and to cause turnover and remodeling of the eye and to protect the retina against the harmful effects of cysteine proteases. It is also used to treat immunological disorders, since cystatin F regulated T-cell function.

Antagonists of cystatin F may be used to treat and/or prevent cerebral haemorrhages and leukoencephalopathy, as well as to treat and/or prevent tumors and other neoplasia and to block HIV infection. Cystatin polypeptides, polynucleotides, agonists and antagonists may also be used for gene therapy methods.

ADVANTAGE - The effects of the cystatin family protease inhibitors are varied and influence numerous functions. Therefore, there is a need for identification and characterization of additional cystatins which may be used to treat and prevent disease.

Dwg.0/6

L10 ANSWER 12 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-265938 [23] WPIDS
DOC. NO. CPI: C1999-078574
TITLE: New DNA primase (dnaG) polypeptide and polynucleotide, useful for screening for antibacterial drugs.
DERWENT CLASS: B04 D13 D16
INVENTOR(S): JAWORSKI, D D; LENNOX, A L; MAY, E W; WANG, M; WARREN, R L; LENOX, A L
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BECKMAN CORP
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 915161	A2	19990512	(199923)*	EN	38
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2248169	A1	19990421	(199940)	EN	
JP 11239489	A	19990907	(199947)		97

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 915161	A2	EP 1998-203422	19981009
CA 2248169	A1	CA 1998-2248169	19981020
JP 11239489	A	JP 1998-338366	19981021

PRIORITY APPLN. INFO: US 1997-70912P 19971021
AN 1999-265938 [23] WPIDS
AB EP 915161 A UPAB: 19991122
NOVELTY - An isolated Streptococcus pneumoniae polypeptide (I) of the DNA primase (DnaG) family.

DETAILED DESCRIPTION - (I) is selected from an isolated polypeptide:

(i) comprising or at least 95% identical to the fully defined 591 amino acid sequence given in the specification;

(ii) which is the 591 amino acid sequence; or

(iii) encoded by a recombinant polynucleotide (II) comprising the fully defined 2748 bp sequence given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide selected from a polynucleotide:

(i) comprising or at least 95% identical to (II);

(ii) encoding (I);

(iii) encoding the mature polypeptide expressed by the DnaG gene of Streptococcus pneumoniae;
(iv) obtained by screening a library with a fragment of (II); and
(v) complementary to the above polynucleotides
(2) an antibody antigenic/immunospecific to (I);
(3) an agonist or antagonist of (I);
(4) an expression system comprising (II);
(5) a host cell comprising expression system of (4) or a membrane of;
(6) a method for treatment of an individual:
(i) in need of enhanced activity/expression of (I), by administering:
(a) an agonist of (I); or
(b) polynucleotide (II) in vivo;
(ii) needing to inhibit activity/expression of (I), by administering:
(a) an antagonist of (I);
(b) a nucleic acid molecule that inhibits expression of (II); or
(c) a polypeptide that competes with (I) for its ligand or substrate;
(7) preparation of (I); and
(8) a computer readable medium stored with data selected from:
(i) dnaG polynucleotide (I) or polypeptide (II)
(ii) a set of polynucleotides or polypeptides, where at least one sequence is a dnaG polynucleotide of polypeptide; and
(iii) a data set representing dnaG polynucleotides or polypeptides.

USE - DnaG polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the dnaG gene, or analyzing for the presence or amount of dnaG polypeptide expressed in a patient sample (claimed). DnaG PCR probes are useful for diagnosing diseases, and can characterize the response of the infectious organism to drugs.

DnaG polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious microorganisms. DnaG agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (antagonist or antisense sequence) dnaG activity (claimed), therefore treating microbial diseases, especially Streptococcus pneumoniae diseases including conjunctivitis, pneumonia and meningitis.

Epitopes of dnaG polypeptides and polynucleotides are useful immunogens for producing anti-dnaG antibodies for prevention of bacterial infections, and dnaG polynucleotides can be used in genetic immunization (gene therapy) to prevent infections.

DnaG polynucleotides and polypeptides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

They are also useful as reagents for differential screening methods e.g. using dnaG probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. The are also useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis.

The computer based method (8) is useful for performing homology identification by comparing a polynucleotide with dnaG sequences, and is also useful for polynucleotide assembly, by screening for

overlapping sequences between a polynucleotide and dnaG polynucleotide of (8) (claimed).
Dwg.0/0

L10 ANSWER 13 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-265516 [23] WPIDS
DOC. NO. CPI: C1999-078396
TITLE: New Streptococcus pneumoniae UDP-N-acetylenolpyruvylglucosamine reductase (MurB) polypeptide and polynucleotide, useful for screening for antibiotic, and for diagnosis, prevention and treatment of Streptococci infections e.g. meningitis.
DERWENT CLASS: B01 B04 D16
INVENTOR(S): BISWAS, S; BROWN, J R; CHALKER, A F; HOLMES, D J; INGRAHAM, K A; JAWORSKI, D D; RAY, J; SHILLING, L K; WALLIS, N G; WANG, M; ZALACAIN, M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 911403	A2	19990428	(199923)*	EN	38
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2241403	A	19990225	(199932)		
JP 11221085	A	19990817	(199943)		103
US 6218528	B1	20010417	(200123)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 911403	A2		EP 1998-306699	19980821
CA 2241403	A		CA 1998-2241403	19980821
JP 11221085	A		JP 1998-280412	19980825
US 6218528	B1	Provisional	US 1997-57352P	19970825
			US 1998-78691	19980514

PRIORITY APPLN. INFO: US 1998-78691 19980514; US 1997-57352P 19970825
AN 1999-265516 [23] WPIDS
AB EP 911403 A UPAB: 19990616
NOVELTY - An isolated Streptococcus pneumoniae UDP-N-acetylenolpyruvylglucosamine reductase (MurB) polypeptide comprising a polypeptide sequence at least 70% identical to (I) or (II), fully defined 316 and 229 amino acids sequences respectively, given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide selected from:

(a) an isolated polynucleotide at least 70% identical to a polynucleotide encoding MurB polypeptide (I) or (II), or 70% identical to sequence (III) or (IV), fully defined 1102 and 700 bp sequences respectively, given in the specification;

(b) an isolated polynucleotide encoding a polypeptide at least 70% identical to (I) or (II);

(c) an isolated polynucleotide which is (III) or (IV); and

(d) an isolated polynucleotide encoding the same mature MurB polypeptide expressed by the Streptococcus pneumoniae 0100993 NCIMB 40794/40880 MurB gene;

(2) an antibody antigenic to or immunospecific to MurB (I) or (II);

(3) an agonist or antagonist of MurB (I) or (II) activity or expression;

(4) an expression system comprising a polynucleotide capable of expressing MurB polypeptides;

(5) a host cell or membrane for expression of MurB polypeptides;

(6) use of the host cell for preparation of MurB (I) and (II);

(7) a method for treatment of an individual:

(a) needing enhanced activity/expression of MurB polypeptides by administering:

(i) a MurB agonist; or

(ii) MurB polynucleotides in vivo; or

(b) needing to inhibit activity/expression of MurB polynucleotides by administering:

(i) a MurB antagonist; or

(ii) a nucleic acid molecule which inhibits expression of the MurB polynucleotide; or

(iii) a polypeptide that competes with the MurB polynucleotide for its ligand, substrate or receptor; and

(8) a computer readable medium stored with data selected from:

(a) MurB polynucleotides (III)/(IV) or polypeptides (I)/(II);

(b) a set of polynucleotides or polypeptides, where at least one sequence is a MurB polynucleotide or polypeptide; and

(c) a data set representing MurB polynucleotides or polypeptides.

USE - MurB polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the MurB gene or analyzing for the presence of amount of MurB polypeptide expressed in a patient sample (claimed).

MurB PCR probes are useful for diagnosing diseases, and can characterize the response of the infectious organism to drugs.

MurB polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious microorganisms. MurB agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) MurB activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, conjunctivitis, pneumonia, bacteremia, sinusitis, endocarditis and especially meningitis.

Epitopes of MurB polypeptides and polynucleotides are useful immunogens for producing anti-MurB antibodies for prevention of bacterial infections, and MurB polynucleotides can be used in genetic immunization (gene therapy) to prevent infections. MurB polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

MurB polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using MurB probes in RT-PCR to identify and quantify genes expressed in bacterial

tissue.

MurB polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis.

The computer based method (8) is useful for performing homology identification by comparing a polynucleotide with MurB sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and MurB polynucleotide of (8) (claimed).

Dwg.0/0

L10 ANSWER 14 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-144805 [13] WPIDS
DOC. NO. CPI: C1999-042560
TITLE: New Streptococcus pneumoniae ftsZ polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococci infections which cause bacteremia, otitis media and meningitis.
DERWENT CLASS: B04 D16
INVENTOR(S): FUEYO, J L; LONETTO, M A
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (FUEY-I) FUEYO J L; (LONE-I) LONETTO M A
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 899334	A2	19990303	(199913)*	EN	37
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2239819	A	19990212	(199930)		
JP 11187888	A	19990713	(199938)		33
US 6197300	B1	20010306	(200115)		
US 2002004580	A1	20020110	(200208)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 899334	A2		EP 1998-306077	19980730
CA 2239819	A		CA 1998-2239819	19980807
JP 11187888	A		JP 1998-263872	19980812
US 6197300	B1	Provisional	US 1997-55720P	19970812
			US 1998-120426	19980722
US 2002004580	A1	Provisional	US 1997-55720P	19970812
		Div ex	US 1998-120426	19980722
			US 2001-754608	20010104

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2002004580	A1	Div ex	US 6197300

PRIORITY APPLN. INFO: US 1997-55720P 19970812; US 1998-120426 19980722; US 2001-754608 20010104
AN 1999-144805 [13] WPIDS
AB EP 899334 A UPAB: 19990331

A new Streptococcus pneumoniae ftsZ polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 419 and 223 amino acids proteins respectively, given in the specification; (b) an isolated polypeptide comprising ftsZ sequence (I) or (II); (c) an isolated polypeptide which is sequence (I) or (II); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 1260 and 669 bp nucleic acids respectively, given in the specification. Also claimed are: (1) the isolated ftsZ polynucleotides (III) and (IV); (2) an expression system comprising ftsZ polynucleotides; (3) a host cell comprising the expression system or a membrane of; (4) an antibody antigenic to or immunospecific for the ftsZ polypeptide; (5) an agonist or an antagonist of the ftsZ polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of ftsZ polypeptide by administering: (i) agonist of (5); or (ii) ftsZ polynucleotides in vivo; or (b) needing to inhibit activity/expression of the ftsZ polypeptide by administering: (i) antagonist of (5); or (ii) a nucleic acid molecule which inhibits expression/activity of the ftsZ polynucleotide; or (iii) a polypeptide which competes with the ftsZ polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (a) ftsZ polynucleotides (III)/(IV) or polypeptides (I)/(II); (b) a set of polynucleotides or polypeptides, where at least one sequence is an ftsZ polynucleotide or polypeptide; and (c) a data set representing ftsZ polynucleotides or polypeptides.

USE - FtsZ polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the ftsZ gene or analysing for the presence of amount of ftsZ polypeptide expressed in a patient sample (claimed). FtsZ PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. FtsZ polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms. FtsZ agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) ftsZ activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of ftsZ polypeptides and polynucleotides are useful immunogens for producing anti-ftsZ antibodies for prevention of bacterial infections, and ftsZ polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. ftsZ polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. FtsZ polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using ftsZ probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. FtsZ polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identification by comparing a polynucleotide with ftsZ sequences, and is also useful for polynucleotide assembly, by screening for

overlapping sequences between a polynucleotide and ftsZ polynucleotide of (7) (claimed).
Dwg.0/0

L10 ANSWER 15 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-144800 [13] WPIDS
DOC. NO. NON-CPI: N1999-105363
DOC. NO. CPI: C1999-042555
TITLE: New Streptococcus pneumoniae dexB polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcal infections which cause bacteremia, otitis media and meningitis.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): BURNHAM, M K R
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 899329	A2	19990303	(199913)*	EN	36
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2242252	A	19990302	(199933)		
JP 11253171	A	19990921	(199950)		98
US 6228584	B1	20010508	(200128)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 899329	A2		EP 1998-306698	19980821
CA 2242252	A		CA 1998-2242252	19980825
JP 11253171	A		JP 1998-288630	19980902
US 6228584	B1	Provisional	US 1997-57876P	19970902
			US 1998-137077	19980820

PRIORITY APPLN. INFO: US 1997-57876P 19970902; US 1998-137077 19980820
AN 1999-144800 [13] WPIDS
AB EP 899329 A UPAB: 19990331
A new Streptococcus pneumoniae dexB polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), a fully defined 535 amino acid protein given in the specification; (b) an isolated polypeptide comprising dexB sequence (I); (c) an isolated polypeptide which is sequence (I); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (II), a fully defined 1608 bp nucleic acid given in the specification. Also claimed are: (1) the isolated polynucleotide (II) and its complements encoding dexB polypeptide (I); (2) an expression system comprising dexB polynucleotide; (3) a host cell comprising the expression system or a membrane of; (4) an antibody antigenic to or immunospecific for the dexB polypeptide; (5) an agonist or an antagonist of the dexB polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of dexB polypeptide by

administering: (i) agonist of (5); or (ii) dexB polynucleotides in vivo; or (b) needing to inhibit activity/expression of the dexB polypeptide by administering: (i) antagonist of (5); or (ii) a nucleic acid molecule which inhibits expression/activity of the dexB polynucleotide; or (iii) a polypeptide which competes with the dexB polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (a) dexB polynucleotide (II) or polypeptide (I); (b) a set of polynucleotides or polypeptides, where at least one sequence is a dexB polynucleotide or polypeptide; and (c) a data set representing dexB polynucleotides or polypeptides.

USE - DexB polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the dexB gene or analysing for the presence of amount of dexB polypeptide expressed in a patient sample (claimed). DexB PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. DexB polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms. DexB agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) dexB activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of the dexB polypeptide and polynucleotide are useful immunogens for producing anti-dexB antibodies for prevention of bacterial infections, and the dexB polynucleotide can be used in genetic immunisation (gene therapy) to prevent infections. DexB polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. DexB polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using dexB probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. DexB polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identification by comparing a polynucleotide with dexB sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and dexB polynucleotide of (7) (claimed).

Dwg.0/0

L10 ANSWER 16 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-134240 [12] WPIDS
DOC. NO. NON-CPI: N1999-097908
DOC. NO. CPI: C1999-039472
TITLE: New Phospho-N-acetylmuramoyl-pentapeptide-transferase (mraY) polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Staphylococcus pneumoniae infections, which cause otitis media and meningitis.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): FUEYO, J L; JAWORSKI, D D; KOSMATKA, A L; LONETTO, M A; TRAINI, C M; WANG, M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 897007	A2	19990217	(199912)*	EN	37
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2231728	A	19990212	(199930)		
JP 11146794	A	19990602	(199932)		32
US 6156537	A	20001205	(200066)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 897007	A2		EP 1998-304635	19980611
CA 2231728	A		CA 1998-2231728	19980514
JP 11146794	A		JP 1998-224236	19980807
US 6156537	A	Provisional	US 1997-55467P	19970812
			US 1998-61156	19980416

PRIORITY APPLN. INFO: US 1998-61156 19980416; US 1997-55467P 19970812
AN 1999-134240 [12] WPIDS
AB EP 897007 A UPAB: 19990324

A new isolated Phospho-N-acetylmuramoyl-pentapeptide-transferase (mraY) polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 326 and 207 amino acids proteins respectively, given in the specification; (b) an isolated polypeptide comprising mraY sequence (I) or (II); (c) an isolated polypeptide which is sequence (I) or (II); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 981 and 621 bp nucleic acids respectively, given in the specification. Also claimed are: (1) isolated mraY polynucleotides (III) and (IV); (2) an expression system comprising mraY polynucleotides; (3) a (recombinant) host cell comprising the expression system or a membrane of; (4) an antibody antigenic to or immunospecific for the mraY polypeptide; (5) an agonist or an antagonist (V) of the mraY polypeptide; (6) a met hod for the treatment of an individual: (a) needing enhanced activity/expression of mraY polypeptide by administering: (i) agonist (V); or (ii) mraY polynucleotides in vivo; or (b) needing to inhibit activity/expression of the mraY polypeptide by administering: (i) antagonist (V); or (ii) a nucleic acid molecule which inhibits expression/activity of the mraY polynucleotide; or (iii) a polypeptide which competes with the mraY polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (a) mraY polynucleotides (III)/(IV) or polypeptides (I)/(II); (b) a set of polynucleotides or polypeptides, where at least one sequence is an mraY polynucleotide or polypeptide; and (c) a data set representing mraY polynucleotides or polypeptides.

USE - MraY polynucleotides and polypeptides are useful for

diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the mraY gene or analysing for the presence of amount of mraY polypeptide expressed in a patient sample (claimed). MraY PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. MraY polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms. MraY agonists and antagonists (V) are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) mraY activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of mraY polypeptides and polynucleotides are useful immunogens (vaccines) for producing anti-mraY antibodies for prevention of bacterial infections, and mraY polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. MraY polypeptides, polynucleotides and their (ant)agonists (V) can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. MraY polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using mraY probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. MraY polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identification by comparing a polynucleotide with mraY sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and mraY polynucleotide of (7) (claimed).
Dwg.0/0

L10 ANSWER 17 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-108349 [10] WPIDS
DOC. NO. CPI: C1999-032522
TITLE: New SecA polypeptides and polynucleotides - useful as diagnostic reagents and for prevention and treatment of Streptococcus pneumoniae infections, especially meningitis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): JAWORSKI, D D; ODWYER, K M; SHILLING, L K; TRAINI, C M; WANG, M; WILDING, E I; O'DWYER, K M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 894857	A2	19990203	(199910)*	EN	34
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2238672	A	19990201	(199929)		
JP 11192091	A	19990721	(199939)		83

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 894857	A2	EP 1998-305872	19980723
CA 2238672	A	CA 1998-2238672	19980724
JP 11192091	A	JP 1998-250289	19980731

PRIORITY APPLN. INFO: US 1998-999720 19980313; US 1997-54568P 19970801

AN 1999-108349 [10] WPIDS

AB EP 894857 A UPAB: 19990310

A secA polypeptide at least 70% identical to sequence (I), a fully defined 837 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) complementary or at least 70% identity to a polynucleotide encoding (I); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4); an antibody against secA polypeptide (I); (5) an antagonist which inhibits activity or expression of secA polypeptide (I); (6) an isolated polynucleotide (IV) comprising at least 70% identity to a polynucleotide encoding polypeptide (III), a fully defined 693 amino acid protein given in the specification; and (7) a computer readable medium stored with data selected from: (i) secA polynucleotides (II)/(IV) or polypeptides (I)/(III); (ii) a set of polynucleotides or polypeptides, where at least one sequence is a secA polynucleotide or polypeptide; and (iii) a data set representing secA polynucleotides or polypeptides.

USE - SecA polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the secA gene or analysing for the presence of amount of secA polypeptide expressed in a patient sample (claimed). SecA PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. SecA polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms by binding with secA polypeptide (I) and observing interaction and activation or inhibition of the polypeptide function (claimed). SecA polypeptides and antagonists are useful for treating conditions associated with abnormal secA protein levels (claimed), and secA agonists, antagonists and drugs are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) secA activity, therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of secA polypeptides and polynucleotides are useful immunogens for producing anti-secA antibodies for prevention of bacterial infections, and secA polynucleotides can be used in genetic immunisation (gene therapy)using the vector to prevent infections (claimed). SecA polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. SecA polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using secA probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. SecA polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology

identification by comparing a polynucleotide with secA sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and secA polynucleotide of (7) (claimed).

L10 ANSWER 18 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-083580 [08] WPIDS
DOC. NO. NON-CPI: N1999-060291
DOC. NO. CPI: C1999-025357
TITLE: New Streptococcus pneumoniae Histidine Kinase polypeptides and polynucleotides - useful as diagnostic reagents and for prevention and treatment of Streptococcal infections including meningitis.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): THROUP, J; WALLIS, G N; WALLIS, N G
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 892063	A2	19990120	(199908)*	EN	42
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2237050	A	19990118	(199927)		
JP 11178587	A	19990706	(199937)		36

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 892063	A2	EP 1998-305498	19980710
CA 2237050	A	CA 1998-2237050	19980707
JP 11178587	A	JP 1998-236238	19980717

PRIORITY APPLN. INFO: US 1997-53127P 19970718
AN 1999-083580 [08] WPIDS
AB EP 892063 A UPAB: 19990224
A new bacterial Histidine Kinase (HK) polypeptide which is a component of the two component signal transduction system (TCSTS) is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 365 and 272 amino acids proteins respectively, given in the specification; (b) an isolated polypeptide comprising HK sequence (I) or (II); (c) an isolated polypeptide which is sequence (I) or (II); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 1339 and 850 bp nucleic acids respectively, given in the specification. Also claimed are: (1) an expression system comprising HK polynucleotides; (2) a host cell comprising the expression system or a membrane of; (3) an antibody antigenic to or immunospecific for the HK polypeptide; (4) an agonist or an antagonist of the HK polypeptide; (5) a method for the treatment of an individual: (a) needing enhanced activity/expression of HK polypeptide by administering: (i) agonist of (4); or (ii) HK

polynucleotides in vivo; or (b) needing to inhibit activity/expression of the HK polypeptide by administering: (i) antagonist of (4); or (ii) a nucleic acid molecule which inhibits expression/activity of the HK polynucleotide; or (iii) a polypeptide which competes with the HK polypeptide for its ligand, substrate or receptor; and (6) a computer readable medium stored with data selected from: (a) HK polynucleotides (III)/(IV) or polypeptides (I)/(II); (b) a set of polynucleotides or polypeptides, where at least one sequence is an HK polynucleotide or polypeptide; and (c) a data set representing HK polynucleotides or polypeptides.

USE - HK polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the HK gene or analysing for the presence of amount of HK polypeptide expressed in a patient sample (claimed). HK PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. HK polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms. HK agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) HK activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of HK polypeptides and polynucleotides are useful immunogens for producing anti-HK antibodies for prevention of bacterial infections, and HK polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. HK polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. HK polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using HK probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. HK polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (6) is useful for performing homology identification by comparing a polynucleotide with HK sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and HK polynucleotide of (6).

L10 ANSWER 19 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-083574 [08] WPIDS
DOC. NO. NON-CPI: N1999-060290
DOC. NO. CPI: C1999-025351
TITLE: New Streptococcus pneumoniae response regulator polypeptides and polynucleotides - useful as diagnostic reagents and for prevention and treatment of Streptococcus pneumoniae infections, especially pneumonia, bacteremia and meningitis.
DERWENT CLASS: B04 D16 S03 S05 T01
INVENTOR(S): BISWAS, S; KOSMATKA, A L; SHILLING, L K; THROUP, J; WALLIS, N G; ZALACAIN, M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 892057	A2	19990120	(199908)*	EN	39
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2237043	A	19990118	(199927)		
JP 11206388	A	19990803	(199941)		113

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 892057	A2	EP 1998-305517	19980710
CA 2237043	A	CA 1998-2237043	19980707
JP 11206388	A	JP 1998-236239	19980717

PRIORITY APPLN. INFO: US 1997-53238P 19970718
AN 1999-083574 [08] WPIDS
AB EP 892057 A UPAB: 19990324

A new bacterial response regulator (RR) polypeptide which is a component of the two component signal transduction system (TCSTS) is selected from: (i) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 228 and 207 amino acids proteins respectively, given in the specification; (ii) an isolated polypeptide comprising RR sequence (I) or (II); (iii) an isolated polypeptide which is sequence (I) or (II); and (iv) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 901 and 2025 bp nucleic acids respectively, given in the specification. Also claimed are: (1) polynucleotides (III) and (IV) as above; (2) an expression system comprising RR polynucleotides; (3) a host cell comprising the expression system or a membrane of; (4) an antibody antigenic to or immunospecific for the RR polypeptide; (5) an agonist or an antagonist of the RR polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of RR polypeptide by administering: (i) agonist of (5); or (ii) RR polynucleotides in vivo; or (b) needing to inhibit activity/expression of the RR polypeptide by administering: (i) antagonist of (5); or (ii) a nucleic acid molecule which inhibits expression/activity of the RR polynucleotide; or (iii) a polypeptide which competes with the RR polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (a) RR polynucleotides (III)/(IV) or polypeptides (I)/(II); (b) a set of polynucleotides or polypeptides, where at least one sequence is an RR polynucleotide or polypeptide; and (c) a data set representing RR polynucleotides or polypeptides.

USE - RR polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the RR gene or analysing for the presence of amount of RR polypeptide expressed in a patient sample (claimed). RR PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. RR polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms. RR agonists and antagonists are bacteriostatic and bacteriocidal compounds which

can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) RR activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of RR polypeptides and polynucleotides are useful immunogens for producing anti-RR antibodies for prevention of bacterial infections, and RR polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. RR polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. RR polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using RR probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. RR polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identification by comparing a polynucleotide with RR sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and RR polynucleotide of (7) (claimed).

L10 ANSWER 20 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-072880 [07] WPIDS
DOC. NO. NON-CPI: N1999-053423
DOC. NO. CPI: C1999-021865
TITLE: New Streptococcus aureus UDP-N-acetylglucosamine enolpyruvltransferase (murA) polypeptides and polynucleotides - useful as diagnostic reagents and for prevention and treatment of Streptococcus aureus infections.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): WALLIS, N G
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 890644	A2	19990113	(199907)*	EN	39
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2236493	A	19990110	(199926)		
JP 11137248	A	19990525	(199931)		33

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 890644	A2	EP 1998-305253	19980701
CA 2236493	A	CA 1998-2236493	19980706
JP 11137248	A	JP 1998-229901	19980710

PRIORITY APPLN. INFO: US 1997-52214P 19970710
AN 1999-072880 [07] WPIDS

AB EP 890644 A UPAB: 19990217
A new UDP-N-acetylglucosamine enolpyruvyltransferase (MurA) polypeptide which catalyses the first step of peptidoglycan biosynthesis, needed for bacterial growth, is selected from: (i) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 421 and 252 amino acids proteins respectively, given in the specification; (ii) an isolated polypeptide comprising MurA sequence (I) or (II); (iii) an isolated polypeptide which is MurA sequence (I) or (II); and (iv) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 1634 and 1050 bp nucleic acids respectively, given in the specification. Also claimed are: (1) an isolated polynucleotide complementary or at least 70-95% identical to sequences (III) or (IV) encoding polypeptide (I) and (II); (2) an expression system comprising MurA polynucleotide (III) or (IV); (3) a host cell comprising the expression system or membrane, and a transformed host cell; (4) an antibody immunospecific for the MurA polypeptide; (5) an agonist or antagonist of the MurA polypeptide; (6) a method for the treatment of an individual: (i) needing enhanced activity/expression of MurA polypeptide by administering: (a) agonist of (5); or (b) MurA polynucleotide (III) or (IV) in vivo; or (ii) needing to inhibit activity/expression of the MurA polypeptide by administering: (a) antagonist of (5); or (b) a nucleic acid molecule which inhibits expression of the MurA polynucleotide; or (c) a polypeptide which competes with the MurA polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (i) MurA polynucleotides (III)/(IV); (ii) a set of polynucleotides ar polypeptides, where at least one sequence is a MurA polynucleotide or polypeptide; and (iii) a data set representing MurA polynucleotides or polypeptides.

USE - MurA polypeptides and polynucleotides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the MurA gene or analysing for the presence or amount of MurA polypeptide expressed in a patient (claimed). MurA PCR probes are useful for diagnosing diseases, and can characterise the stage and species or strain causing the infection. The MurA probes can also determine the response of the infectious organism to drugs. MurA polypeptides and polynucleotides are useful for screening for antagonists, agonists and drugs against infection from micro-organisms. MurA agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) MurA activity, therefore **treating** bacterial infections, especially by **Streptococcus** aureus which causes bacteremia in cancer patients, osteomyelitis, septic arthritis, septic thrombophlebitis, acute bacterial endocarditis, toxic shock syndrome, scalded skin syndrome and Staphylococcal food poisoning. Epitopes of MurA polypeptides and polynucleotides are useful immunogens for producing anti-MurA antibodies for prevention of bacterial infections, and MurA polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. MurA polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. MurA polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using probes in RT-PCR to

identify and quantify genes expressed in bacterial infected tissue. MurA polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identifiaction by comparing a polynucleotide with MurA sequences (7), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and MurA polynucleotides (6) (claimed).

L10 ANSWER 21 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-062663 [06] WPIDS
DOC. NO. NON-CPI: N1999-046543
DOC. NO. CPI: C1999-018845
TITLE: New isolated gidA2 polypeptide from Streptococcus pneumoniae - used to diagnose, treat and prevent bacterial infections e.g. S. pneumoniae and meningitis and H. pylori and related cancers, ulcers and gastritis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): FEDON, J C; KALLENDER, H; LENOX, A L; PALMER, L M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 889132	A2	19990107	(199906)*	EN	42
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2236441	A	19990101	(199924)		
JP 11137266	A	19990525	(199931)		109
JP 2000050890	A	20000222	(200020)		37

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 889132	A2		EP 1998-305208	19980630
CA 2236441	A		CA 1998-2236441	19980629
JP 11137266	A		JP 1998-223539	19980701
JP 2000050890	A	Div ex	JP 1998-223539	19980701
			JP 1999-212084	19980701

PRIORITY APPLN. INFO: US 1997-51378P 19970701
AN 1999-062663 [06] WPIDS
AB EP 889132 A UPAB: 19990217
New isolated polypeptide (I) is at least 70 % identical with sequences of 444 or 331 amino acids ((2) or (4) respectively) over the entire length, is or includes (2) or (4) or is encoded by recombinant nucleic acids of 1500 or 1195 base pairs ((1) and (3) respectively). Also claimed are: (i) an isolated nucleic acid (II) that encodes (I), is at least 70 % identical with (1) or (3), or other sequences encoding (2) and (4), over the entire length, is or includes (1) or (3), is obtained by screening a library with (1), (3) or their fragments under stringent conditions, encodes the mature polypeptide expressed by the gidA2 gene of Streptococcus

pneumoniae or is complementary to any of the above in (i); (ii) an antibody (Ab) directed against (I); (iii) an agonist or antagonist (III) of the activity or expression of (I); (iv) an expression system for producing (I); (v) a host cell, or derived membranes, containing the above expression system; and (vi) a computer-readable medium having sequence data for (I) and (II) stored on it.

USE - (I), its agonists or (II) are used to treat conditions requiring increased activity or expression of (I), while conditions (particularly bacterial infections) requiring inhibition of such activity or expression are treated by administering an **antagonist**, inhibitory nucleic acid or competitive polypeptide. Especially infection by **S. pneumoniae** (e.g. meningitis) is **treated**, but also H. pylori infections (and related cancers, ulcers and gastritis). These antibacterial agents may also be used to treat in-dwelling devices to prevent infection or generally as wound treatments to prevent adhesion of bacteria to matrix proteins. (I)-related conditions, or susceptibility to them, can be diagnosed, staged or prognosed by detecting mutations in (I)-encoding nucleic acid or by determining the presence or amount of (I). (I) or cell membranes of (v) are used to screen for (II) (in any standard binding assay) and cells of (v) are used to produce recombinant (I), used to raise Ab (for use in identifying/isolating (I)-expressing clones, for affinity purification, as therapeutic agent and in competitive drug screens), to identify (III) or specific receptors, in rational drug design and as immunogens for vaccines. (II) or its fragments are used as antisense/ribozyme therapeutics, as probes and primers to isolate homologous sequences, to detect (mutant) (II), for chromosomal mapping, to determine bacterial serotypes, for genetic immunisation, to screen for (III) and in rational drug design. The medium of (vi) is used to identify homologous sequences and in computer-based polynucleotide assembly (by detecting overlapping regions between different sequences). The active agents are administered e.g. topically, orally or by injection at a dosage of 0.01-10 (preferably 1) mg/kg and vaccinating doses of antigens are 0.5-5 mu g/kg, given 1-3 times at intervals of 1-3 weeks.

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L10 ANSWER 22 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-001403 [01] WPIDS
DOC. NO. NON-CPI: N1999-001244
DOC. NO. CPI: C1999-000473
TITLE: New Streptococcus pneumoniae Histidine kinase polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcal and Heliobacter pylori infections.
DERWENT CLASS: B04 D16 T01
INVENTOR(S): BISWAS, S; THROUP, J P; ZALACAIN, M; THROUP, J; WALLIS, N; BROWN, J R; WALLIS, N G
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 881297	A2	19981202	(199901)*	EN	40

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CA 2233577	A	19981130 (199920)	
JP 11113582	A	19990427 (199927)	106
US 6165991	A	20001226 (200103)	
US 6287836	B1	20010911 (200154)	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 881297	A2		EP 1998-304216	19980528
CA 2233577	A		CA 1998-2233577	19980528
JP 11113582	A		JP 1998-188023	19980529
US 6165991	A	Provisional	US 1997-48346P	19970530
		CIP of	US 1997-878858	19970620
		CIP of	US 1997-947251	19971008
			US 1998-80963	19980519
US 6287836	B1	Provisional	US 1997-48346P	19970530
		CIP of	US 1997-878858	19970620
			US 1997-947251	19971008

PRIORITY APPLN. INFO: US 1997-48346P 19970530; US 1997-878858 19970620; US 1997-947251 19971008; US 1998-80963 19980519

AN 1999-001403 [01] WPIDS

AB EP 881297 A UPAB: 19990107

A new bacterial Histidine kinase (HK) polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70 (especially 95)% identity to sequence (II), and 70 (especially 99)% identity to sequence (IV), fully defined 350 and 159 amino acid proteins respectively, given in the specification; (b) an isolated polypeptide comprising HK sequence (II) or (IV); (c) an isolated polypeptide which is HK sequence (II) or (IV); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (I) or (III), fully defined 1199 and 480bp nucleic acids respectively, given in the specification. Also claimed are: (1) an isolated polynucleotide of (d) comprising a nucleic acid sequence encoding a polypeptide with 70 (especially 95)% identity to sequences (II) or (IV); (2) an expression system comprising polynucleotide (d); (3) a host cell comprising expression system or a membrane of (2); (4) an antibody antigenic to or immunospecific for the HK polypeptide; (5) an agonist or an antagonist of the HK polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of HK polypeptide b y administering (i) an agonist (5); or (ii) HK polynucleotide (d) in vivo; or (b) needing to inhibit activity/expression of the HK polypeptide by administering (i) an antagonist (5); (ii) a nucleic acid molecule which inhibits expression of the HK polynucleotide; or (iii) a polypeptide which competes with the HK polypeptide for its ligand, substrate or receptor; (7) a process for diagnosing or prognosing a disease or susceptibility to a disease by determining the presence or absence of a mutation in HK polynucleotide (d)/(1), or analysing the presence or amount of HK polynucleotide (d)/(1); and (8) a computer readable medium stored with data selected from: (a) HK polynucleotides (I)/(III) or polypeptides (II)/(IV); (b) a set of polynucleotides or polypeptides, where at least one sequence

is an HK polynucleotide or polypeptide; and (c) a data set representing HK polynucleotides or polypeptides.

USE - HK polynucleotides and polypeptide are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the HK gene or analysing for the presence or amount of HK polypeptide expressed in a patient sample (claimed). HK PCR probes are useful for diagnosing diseases (especially Streptococcal), and can characterise the stage and the species or strain causing the infection. The HK probes can also determine the response of the infectious organism to drugs. HK polypeptides and polynucleotides are useful for screening for antagonists, agonists and drugs against infectious micro-organisms. HK agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) HK activity, therefore **treating** microbial (especially **Streptococcal**) diseases, ulcers and gastritis, and stomach cancer caused by Heliobacter pylori. Epitopes of HK polypeptides and polynucleotides are useful immunogens for producing anti-HK antibodies for vaccines to prevent bacterial infections, and HK polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. HK polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. HK polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using HK probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. HK polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (8) is useful for performing homology identification by comparing a polynucleotide with HK sequences (8), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and HK polynucleotide (8) (claimed).

L10 ANSWER 23 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-001402 [01] WPIDS
DOC. NO. NON-CPI: N1999-001243
DOC. NO. CPI: C1999-000472
TITLE: New Streptococcus pneumoniae Histidine kinase polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcal and Heliobacter pylori infections.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): BISWAS, S; BRYANT, A; GE, J Y; HOLMES, D J; INGRAHAM, K A; JAWORSKI, D D; MARRA, A; SHILLING, L K; THROUP, J P; WALLIS, N G; WANG, M; ZALACAIN, M; HOLMES, D; INGRAHAM, K; JAWORSKI, D; SHILLING, L; THROUP, J; WALLIS, N
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 881296	A2	19981202	(199901)*	EN	46

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2233547 A 19981130 (199920)
JP 11113581 A 19990427 (199927) 118

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 881296	A2	EP 1998-304211	19980528
CA 2233547	A	CA 1998-2233547	19980528
JP 11113581	A	JP 1998-188021	19980529

PRIORITY APPLN. INFO: US 1997-48339P 19970530
AN 1999-001402 [01] WPIDS
AB EP 881296 A UPAB: 19990210
A new bacterial Histidine kinase (HK) polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70 (especially 95)% identity to sequence (II), and 70 (especially 99)% identity to sequence (IV), fully defined 446 and 321 amino acid proteins respectively, given in the specification; (b) an isolated polypeptide comprising HK sequence (II) or (IV); (c) an isolated polypeptide which is sequence (II) or (IV); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (I) or (III), fully defined 1458 and 2279 bp nucleic acids given in the specification. Also claimed are: (1) an isolated polynucleotide of (d) comprising a nucleic acid sequence encoding a polypeptide with 70 (especially 95)% identity to sequences (II) or (IV); (2) an expression system comprising polynucleotide (d)/(1); (2) a host cell comprising expression system or membrane of (2); (4) an antibody antigenic to or immunospecific for the HK polypeptide; (5) an agonist or an antagonist of the HK polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of HK polypeptide by administering (i) an agonist (5); or (ii) HK polynucleotide (d)/(1) in vivo; or (b) needing to inhibit activity/expression of the HK polypeptide by administering (i) an antagonist (5); or (ii) a nucleic acid molecule which inhibits expression of the HK polynucleotide; or (iii) a polypeptide which competes with the HK polypeptide for its ligand, substrate or receptor; and (8) a computer readable medium stored with data selected from: (a) HK polynucleotides (I)/(III) or polypeptides (II)/(IV); (b) a set of polynucleotides or polypeptides, where at least one sequence is an HK polynucleotide or polypeptide; and (c) a data set representing HK polynucleotides or polypeptides.

USE - HK polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the HK gene or analysing for the presence or amount of HK polypeptide expressed in a patient sample (claimed). HK PCR probes are useful for diagnosing diseases (especially Streptococcal), and can characterise the stage and the species or strain causing the infection. The HK probes can also determine the response of the infectious organism to drugs. HK polypeptides and polynucleotides are useful for screening for antagonists, agonists and drugs against infectious micro-organisms. HK agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (

antagonist or antisense sequence) HK activity, therefore **treating** microbial (especially **Streptococcal**) diseases, ulcers and gastritis and stomach ulcers caused by Heliobacter pylori. Epitopes of HK polypeptides and polynucleotides are useful immunogens for producing anti-HK antibodies for vaccines to prevent bacterial infections, and HK polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. HK polypeptides and polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. HK polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using HK probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. HK polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (8) is useful for performing homology identification by comparing a polynucleotide with HK sequences (8), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and HK polynucleotide (8) (claimed).

L10 ANSWER 24 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-001401 [01] WPIDS
DOC. NO. NON-CPI: N1999-001242
DOC. NO. CPI: C1999-000471
TITLE: New Streptococcus pneumoniae Histidine kinase polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcal and Heliobacter pylori infections.
DERWENT CLASS: B04 D16 T01
INVENTOR(S): BISWAS, S; BRYANT, A; GE, J Y; HOLMES, D J; INGRAHAM, K A; MARRA, A; THROUP, J; WALLIS, N G; ZALACAIN, M; HOLMES, D; INGRAHAM, K; WALLIS, N
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 881295	A2	19981202	(199901)*	EN	42
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2233580	A	19981130	(199920)		
JP 11098990	A	19990413	(199925)		37

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 881295	A2	EP 1998-304206	19980528
CA 2233580	A	CA 1998-2233580	19980528
JP 11098990	A	JP 1998-188022	19980529

PRIORITY APPLN. INFO: US 1997-48345P 19970530
AN 1999-001401 [01] WPIDS

AB EP 881295 A UPAB: 19990122
A new bacterial Histidine kinase (HK) polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having at least 70 (especially 95)% identity to sequence (II), and 70 (especially 99)% identity to sequence (IV), fully defined 443 and 307 amino acid proteins respectively, given in the specification; (b) an isolated polypeptide comprising HK sequence (II) or (IV); (c) an isolated polypeptide which is sequence (II) or (IV); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (I) or (III), fully defined 1395 and 984 bp nucleic acids given in the specification. Also claimed are: (1) an isolated polynucleotide of (d) comprising a nucleic acid (d) sequence encoding a polypeptide with 70 (especially 95)% identity to sequences (II) or (IV); (2) an expression system comprising polynucleotide (d)/(1); (3) a host cell comprising expression system or membrane of (2); (4) an antibody antigenic or immunospecific for the HK polypeptide; (5) an agonist or an antagonist of the HK polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of HK polypeptide by administering: (i) an agonist (5); or (ii) HK polynucleotide (d)/(1) in vivo; or (b) needing to inhibit activity/expression of the HK polypeptide by administering (i) an antagonist (5); or (ii) a nucleic acid molecule which inhibits expression of the HK polynucleotide; or (iii) a polypeptide which competes with the HK polypeptide for its ligand, substrate or receptor; and (8) a computer readable medium stored with data selected from: (a) HK polynucleotides (I)/(III) or polypeptides (II)/(IV); (b) a set of polynucleotides or polypeptides, where at least one sequence is an HK polynucleotide or polypeptide; and (c) a data set representing HK polynucleotides or polypeptides.

USE - HK polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the HK gene or analysing for the presence or amount of HK polypeptide expressed in a patient sample (claimed). HK PCR probes are useful for diagnosing diseases (especially Streptococcal), and can characterise the stage and the species or strain causing the infection. The HK probes can also determine the response of the infectious organism to drugs. HK polypeptides and polynucleotides are useful for screening for antagonists, agonists and drugs against infectious micro-organisms. HK agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) HK activity, therefore **treating** microbial diseases, especially **Streptococcal** and stomach cancer caused by Heliobacter pylori, and ulcers and gastritis caused by other microbial diseases. Epitopes of HK polypeptides and polynucleotides are useful immunogens for producing anti-HK antibodies for prevention of bacterial infections, and HK polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. HK polypeptides and polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. HK polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using HK probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. HK polypeptides are useful for mapping the genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer

based method (8) is useful for performing homology identification by comparing a polynucleotide with HK sequences (8), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and HK polynucleotide (8) (claimed).

L10 ANSWER 25 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-001392 [01] WPIDS
DOC. NO. NON-CPI: N1999-001236
DOC. NO. CPI: C1999-000462
TITLE: New Streptococcus pneumoniae Histidine kinase polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcal and Heliobacter pylori infections.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BISWAS, S; THROUP, J P; WALLIS, N G; ZALACAIN, M; THROUP, J
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC; (BISW-I) BISWAS S; (THRO-I) THROUP J P; (WALL-I) WALLIS N G; (ZALA-I) ZALACAIN M
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 881286	A2	19981202	(199901)*	EN	44
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CA 2233572	A	19981130	(199920)		
JP 11103868	A	19990420	(199926)		112
US 6165992	A	20001226	(200103)		
US 2001020010	A1	20010906	(200154)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 881286	A2		EP 1998-304138	19980526
CA 2233572	A		CA 1998-2233572	19980528
JP 11103868	A		JP 1998-188024	19980529
US 6165992	A	Provisional	US 1997-48347P	19970530
			US 1998-81689	19980520
US 2001020010	A1	Provisional	US 1997-48347P	19970530
		Div ex	US 1998-81689	19980520
			US 2000-737068	20001214

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2001020010	A1	Div ex	US 6165992

PRIORITY APPLN. INFO: US 1997-48347P 19970530; US 1998-81689 19980520; US 2000-737068 20001214
AN 1999-001392 [01] WPIDS
AB EP 881286 A UPAB: 19990113
A new bacterial Histidine kinase (HK) polypeptide is selected from: (a) an isolated polypeptide comprising an amino acid sequence having

at least 70 (especially 95)% identity to sequence (II), and 70 (especially 99)% identity to sequence (IV), fully defined 442 and 248 amino acid proteins respectively, given in the specification; (b) an isolated polypeptide comprising HK sequence (II) or (IV); (c) an isolated polypeptide which is sequence (II) or (IV); and (d) a polypeptide encoded by a recombinant polynucleotide comprising sequence (I) or (III), fully defined 1526 and 1260 bp nucleic acids given in the specification. Also claimed are: (1) an isolated polynucleotide of (d) comprising a nucleic acid sequence encoding a polypeptide with 70 (especially 95)% identity to sequences (II) or (IV); (2) an expression system comprising polynucleotide (d)/(1); (3) a host cell comprising expression system or membrane of (2); (4) an antibody antigenic to or immunospecific for the HK polypeptide; (5) an agonist or antagonist of the HK polypeptide; (6) a method for the treatment of an individual: (a) needing enhanced activity/expression of HK polypeptide by administering (i) an agonist (5); or (ii) HK polynucleotide (d) in vivo; or (b) needing to inhibit activity/expression of the HK polypeptide by administering (i) an antagonist (5); or (ii) a nucleic acid molecule which inhibits expression of the HK polynucleotide; or (iii) a polypeptide which competes with the HK polypeptide for its ligand, substrate or receptor; (7) a process for diagnosing or prognosing a disease or susceptibility to a disease by determining the presence or absence of a mutation in HK polynucleotide (d)/(1), or analysing the presence or amount of HK polypeptide expression; and (8) a computer readable medium stored with data selected from: (a) HK polynucleotides (I)/(III) or polypeptides (II)/(IV); (b) a set of polynucleotides or polypeptides, where at least one sequence is an HK polynucleotide or polypeptide; and (c) a data set representing HK polynucleotides or polypeptides.

USE - HK polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the HK gene or analysing for the presence or amount of HK polypeptide expressed in a patient sample (claimed). HK PCR probes are useful for diagnosing diseases (especially Streptococcal), and can characterise the stage and the species or strain causing the infection. The HK probes can also determine the response of the infectious organism to drugs. HK polypeptides and polynucleotides are useful for screening for antagonists, agonists and drugs against infectious micro-organisms. HK agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) HK activity, therefore **treating** microbial (especially **Streptococcal**) diseases, ulcers and gastritis, and stomach cancer caused by Heliobacter pylori. Epitopes of HK polypeptides and polynucleotides are useful immunogens for producing anti-HK antibodies for vaccines to prevent bacterial infections, and HK polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. HK polypeptides and polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. HK polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using HK probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. HK polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (8) is useful for performing homology

identification by comparing a polynucleotide with HK sequences (8), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and HK polynucleotide (8) (claimed).

L10 ANSWER 26 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-071221 [07] WPIDS
DOC. NO. NON-CPI: N1999-052061
DOC. NO. CPI: C1999-021286
TITLE: New Streptococcus pneumoniae licD1 polypeptides and polynucleotides - useful as diagnostic reagents and for prevention and treatment of Streptococcus pneumoniae infections.
DERWENT CLASS: B04 D16 S03 T01 T03
INVENTOR(S): LONETTO, M A
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (LONE-I) LONETTO M A
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2230473	A	19980828	(199907)*		50
JP 10327883	A	19981215	(199909)		22
EP 908514	A1	19990414	(199919)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
US 6228838	B1	20010508	(200128)		
US 2002102701	A1	20020801	(200253)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
CA 2230473	A		CA 1998-2230473	19980225
JP 10327883	A		JP 1998-90548	19980227
EP 908514	A1		EP 1998-301447	19980227
US 6228838	B1	Provisional	US 1997-39581P	19970228
			US 1998-24024	19980216
US 2002102701	A1	Provisional	US 1997-39581P	19970228
		Div ex	US 1998-24024	19980216
			US 2001-820408	20010329

PRIORITY APPLN. INFO: US 1997-39581P 19970228; US 1998-24024 19980216; US 2001-820408 20010329
AN 1999-071221 [07] WPIDS
AB CA 2230473 A UPAB: 19990217
A licD1 polypeptide comprising at least 70% identity to sequence (I), a fully defined 267 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) complementary or at least 70% identical to a polynucleotide encoding (I); (2) a vector comprising the licD1 polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody antigenic to or immunospecific for the licD1 polypeptide; (4) an antagonist of the licD1 polypeptide; (5) an isolated polynucleotide (IV) at least 70% identical to a polynucleotide encoding polypeptide (III), a fully defined 100 amino

acid sequence given in the specification; and (6) a computer readable medium stored with data selected from: (a) licD1 polynucleotides (II)/(IV) or polypeptides (I)/(III); (b) a set of polynucleotides or polypeptides, where at least one sequence is an licD1 polynucleotide or polypeptide; and (c) a data set representing licD1 polynucleotides or polypeptides.

USE - LicD1 polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the licD1 gene or analysing for the presence of amount of HlicD1polypeptide expressed in a patient sample (claimed). LicD1 PCR probes are useful for diagnosing diseases, and can characterise the response of the infectious organism to drugs. LicD1 polypeptides and polynucleotides are also useful for screening for antagonists, agonists and drugs against infectious micro-organisms. LicD1 agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (**antagonist** or antisense sequence) licD1 activity (claimed), therefore **treating** microbial diseases, especially **Streptococcus pneumoniae** diseases including otitis media, bacteremia, conjunctivitis, pneumonia, sinusitis, pleural empyema, endocarditis and especially meningitis. Epitopes of licD1 polypeptides and polynucleotides are useful immunogens for producing anti-licD1 antibodies for prevention of bacterial infections, and licD1 polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. LicD1 polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. LicD1 polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using licD1 probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. LicD1 polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (6) is useful for performing homology identification by comparing a polynucleotide with licD1 sequences, and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and licD1 polynucleotide of (6) (claimed).

Dwg.0/0

L10 ANSWER 27 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1998-008794 [01] WPIDS
CROSS REFERENCE: 1998-008793 [01]; 1998-322654 [28]; 1999-327408 [27]
DOC. NO. CPI: C1998-003120
TITLE: DNA encoding peptide releasing factor, RF-1 from Streptococcus pneumoniae - useful for diagnosis and treatment of, e.g. otitis media, conjunctivitis and meningitis, etc..
DERWENT CLASS: B04 D16
INVENTOR(S): BLACK, M T; HODGSON, J E; KNOWLES, D J C; NICHOLAS, R O; STODOLA, R K; BURNHAM, M K R; LONETTO, M A; REID, R H; ZARFOS, P N
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9743304	A1	19971120	(199801)*	EN	41
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 914330	A1	19990512	(199923)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 2000512487	W	20000926	(200051)		49
US 6165989	A	20001226	(200103)		
US 6294661	B1	20010925	(200158)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9743304	A1		WO 1997-US8272	19970514
EP 914330	A1		EP 1997-927647	19970514
			WO 1997-US8272	19970514
JP 2000512487	W		JP 1997-541128	19970514
			WO 1997-US8272	19970514
US 6165989	A	Provisional	US 1996-17670P	19960514
		Provisional	US 1996-31879P	19961127
		CIP of	US 1997-858207	19970514
			WO 1997-US8272	19970514
		CIP of	US 1997-919573	19970710
			US 1997-935307	19970922
US 6294661	B1	Provisional	US 1996-17670P	19960514
			WO 1997-US8272	19970514
			US 1999-155920	19990305

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 914330	A1	Based on	WO 9743304
JP 2000512487	W	Based on	WO 9743304
US 6294661	B1	Based on	WO 9743304

PRIORITY APPLN. INFO: US 1996-17670P 19960514; US 1996-31879P 19961127; US 1997-858207 19970514; US 1997-919573 19970710; US 1997-935307 19970922; US 1999-155920 19990305

AN 1998-008794 [01] WPIDS

CR 1998-008793 [01]; 1998-322654 [28]; 1999-327408 [27]

AB WO 9743304 A UPAB: 20020725

A polypeptide comprising an amino acid sequence at least 70% identical to a 359 amino acid residue sequence (A) given in the specification is claimed.

USE - A mutation in S. typhimurium prfA has been demonstrated to inhibit cell division through a novel regulatory circuit. Hence, RF-1 may be used as an anti-bacterial target. In particular (A) can be used to identify compounds which interact with and inhibit or activate the activity of (A) (claimed). **Antagonists** can be used to **treat** disease caused by **S. pneumoniae**. (A) or (I), through genetic immunisation, can also be used to induce an immunological response in a mammal by inoculation with (A) or delivery of (I) in a nucleic acid vector, adequate to produce antibody and/or T cell immune responses to

protect the animal from disease (claimed). The products and methods are particularly useful for diagnosis of disease, preferably, bacterial infections caused by S. pneumoniae, especially otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema and endocarditis.
Dwg.0/0

L10 ANSWER 28 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1998-008793 [01] WPIDS
CROSS REFERENCE: 1998-008794 [01]; 1998-322654 [28]; 1999-327408 [27]
DOC. NO. CPI: C1998-003119
TITLE: Novel Streptococcus pneumoniae proteins and related DNA - useful for diagnosing anti-microbial agents for treatment of bacterial infections.
DERWENT CLASS: B04 D16
INVENTOR(S): BLACK, M T; HODGSON, J E; KNOWLES, D J C; NICHOLAS, R O; STODOLA, R K
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9743303	A1	19971120	(199801)*	EN	483
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 934336	A1	19990811	(199936)	EN	
R: BE CH DE DK FR GB IT LI NL					
JP 2000508178	W	20000704	(200037)		697
US 6348328	B1	20020219	(200221)#		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9743303	A1	WO 1997-US7950	19970514
EP 934336	A1	EP 1997-925516	19970514
		WO 1997-US7950	19970514
JP 2000508178	W	JP 1997-540991	19970514
		WO 1997-US7950	19970514
US 6348328	B1	US 1997-858207	19970514

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 934336	A1	Based on	WO 9743303
JP 2000508178	W	Based on	WO 9743303

PRIORITY APPLN. INFO: US 1996-17670P 19960514; US 1997-858207 19970514
AN 1998-008793 [01] WPIDS
CR 1998-008794 [01]; 1998-322654 [28]; 1999-327408 [27]
AB WO 9743303 A UPAB: 20020725
A novel polypeptide comprises an amino acid sequence at least 70% identical to one of 290 amino acid sequences (A) (all given in the

specification).

USE - (A) are Streptococcus pneumoniae proteins which can be used to identify compounds which interact with and inhibit or activate the activity of (A) (claimed). **Antagonists** can be used to **treat** disease caused by **S. pneumoniae** (A) or (I), through genetic immunisation, can also be used to induce an immunological response in a mammal by inoculation with (A) or delivery of (I) in a nucleic acid vector, adequate to produce antibody and/or T cell immune responses to protect the animal from disease. (A) can also be used to identify antimicrobial compounds (claimed) which are capable of inhibiting the bioactivity of (A). (All claimed). In particular the proteins of the invention can be used to prevent adhesion of bacteria to mammalian extracellular matrix proteins on in-dwelling devices or in wounds, to block protein-mediated mammalian cell invasion, and to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or other surgical techniques.

Dwg.0/0

L10 ANSWER 29 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-549687 [50] WPIDS
CROSS REFERENCE: 1999-356838 [30]
DOC. NO. NON-CPI: N1997-458314
DOC. NO. CPI: C1997-175326
TITLE: DNA encoding response regulator protein of Streptococcus pneumoniae NCIMB 40794 - useful for treatment, prevention, by vaccination, and diagnosis of infection, especially meningitis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): WALLIS, N G
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9741156	A1	19971106	(199750)*	EN	40
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
US 5773250	A	19980630	(199833)		19
EP 934340	A1	19990811	(199936)	EN	
R: BE CH DE DK FR GB IT LI NL					
US 6001362	A	19991214	(200005)		
JP 2000509985	W	20000808	(200043)		49

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9741156	A1		WO 1997-US7383	19970501
US 5773250	A		US 1997-850118	19970501
EP 934340	A1		EP 1997-925429	19970501
			WO 1997-US7383	19970501
US 6001362	A	Div ex	US 1997-850118	19970501
			US 1998-93335	19980608
JP 2000509985	W		JP 1997-539239	19970501

WO 1997-US7383 19970501

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 934340	A1	Based on	WO 9741156
US 6001362	A	Div ex	US 5773250
JP 2000509985	W	Based on	WO 9741156

PRIORITY APPLN. INFO: GB 1996-9021 19960501
AN 1997-549687 [50] WPIDS
CR 1999-356838 [30]
AB WO 9741156 A UPAB: 20000907
A new nucleic acid (I): (a) has at least 70% identity with a sequence encoding a 234 amino acid (aa) sequence (given in the specification), or is its complement; (b) has at least 70% identity with a sequence encoding the same mature polypeptide as that expressed by the response regulator (RR) gene of Streptococcus pneumoniae 0100993 (NCIMB 40794); or (c) contains at least 15 sequential bases of (a) or (b). Also new are (1) vectors containing (I); (2) host cells containing such vectors; (3) polypeptides as above or at least 70% homologous; (4) antibodies (Ab) against (3); (4) antagonists that inhibit activity or expression of (3); and (5) diagnosis of disease related to expression or activity of (3) by determining the sequence of the nucleic acid encoding it or analysing for the presence or amount of (3).

USE - (I) is used to produce recombinant RR or their fragments, as probes or primers to isolate related nucleic acid (e.g. full-length clones), for diagnosis or staging of infection, to detect mutations and polymorphisms in the RR gene, to identify S. pneumoniae, to develop antibacterials and to express antisense nucleic acid. (I), or its fragments encoding non-variable regions of a bacterial cell surface protein, can be used in animal models of infection to determine immunologically active epitopes for subsequent production of therapeutic monoclonal antibodies. RR is used to treat conditions requiring RR polypeptide, while conditions requiring inhibition of RR are treated with **antagonists**, particularly those that are antibacterial, preferably for **treating S. pneumoniae** infection, specifically meningitis. Inoculation with RR, or its fragments, induces an immune response (humoral and/or cellular) that protects against infection. The same result is achieved by expressing RR from a nucleic acid vector in vivo (genetic immunisation). RR are also used to identify antagonists and to generate Ab. The products may also be used to inhibit adhesion of bacteria to extracellular matrix in/on e.g. wound surfaces or in-dwelling devices such as prostheses (which can be soaked in a solution of RR before implanting).
Dwg.0/0

L10 ANSWER 30 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-549672 [50] WPIDS
DOC. NO. NON-CPI: N1997-458312
DOC. NO. CPI: C1997-175311
TITLE: DNA encoding response regulator protein of Streptococcus pneumoniae NCIMB 40794 - useful for treatment, prevention, by vaccination, and diagnosis of infection, especially meningitis.

DERWENT CLASS: B04 D16 S03
INVENTOR(S): WALLIS, N G
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9741135	A1	19971106	(199750)*	EN	43
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
US 5766878	A	19980616	(199831)		
EP 900229	A1	19990310	(199914)	EN	
R: BE CH DE DK FR GB IT LI NL					
US 5880262	A	19990309	(199917)		
JP 2000512485	W	20000926	(200051)		54

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9741135	A1		WO 1997-US7381	19970501
US 5766878	A		US 1997-848932	19970501
EP 900229	A1		EP 1997-925427	19970501
			WO 1997-US7381	19970501
US 5880262	A	Div ex	US 1997-848932	19970501
			US 1998-8180	19980116
JP 2000512485	W		JP 1997-539237	19970501
			WO 1997-US7381	19970501

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 900229	A1	Based on	WO 9741135
US 5880262	A	Div ex	US 5766878
JP 2000512485	W	Based on	WO 9741135

PRIORITY APPLN. INFO: GB 1996-9125 19960501
AN 1997-549672 [50] WPIDS
AB WO 9741135 A UPAB: 19971217
A new nucleic acid (I): (a) has at least 70% identity with a sequence encoding a 210 or 192 amino acid (aa) sequence (given in the specification), or is their complements; (b) has at least 70% identity with a sequence encoding the same mature polypeptide as that expressed by the response regulator (RR) gene of Streptococcus pneumoniae 0100993 (NCIMB 40794); or (c) contains at least 15 sequential bases of (a) or (b). Also new are (1) vectors containing (I); (2) host cells containing such vectors; (3) polypeptides as above or at least 70% homologous; (4) antibodies (Ab) against (3); (4) antagonists that inhibit activity or expression of (3); and (5) diagnosis of disease related to expression or activity of (3) by determining the sequence of the nucleic acid encoding it or analysing for the presence or amount of (3).

USE - (I) is used to produce recombinant RR or their fragments, as probes or primers to isolate related nucleic acid (e.g. full-length clones), for diagnosis or staging of infection, to

detect mutations and polymorphisms in the RR gene, to identify S. pneumoniae, to develop antibacterials and to express antisense nucleic acid. (I), or its fragments encoding non-variable regions of a bacterial cell surface protein, can be used in animal models of infection to determine immunologically active epitopes for subsequent production of therapeutic monoclonal antibodies. RR is used to treat conditions requiring RR polypeptide, while conditions requiring inhibition of RR are treated with **antagonists**, particularly those that are antibacterial, preferably for **treating S. pneumoniae** infection, specifically meningitis. Inoculation with RR, or its fragments, induces an immune response (humoral and/or cellular) that protects against infection. The same result is achieved by expressing RR from a nucleic acid vector in vivo (genetic immunisation). RR are also used to identify antagonists and to generate Ab. The products may also be used to inhibit adhesion of bacteria to extracellular matrix in/on e.g. wound surfaces or in-dwelling devices such as prostheses (which can be soaked in a solution of RR before implanting). Dwg.0/0

L10 ANSWER 31 OF 34 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1995-357434 [46] WPIDS
DOC. NO. CPI: C1995-156442
TITLE: Preventing or **treating** **Streptococcus pneumoniae** infection - by inhibiting binding to host cells, partic. using an **antagonist** of platelet activating factor receptor.
DERWENT CLASS: B04
INVENTOR(S): CUNDELL, D R; GERARD, N P; TUOMANEN, E I
PATENT ASSIGNEE(S): (BETH-N) BETH ISRAEL HOSPITAL ASSOC; (UYRQ) UNIV ROCKEFELLER
COUNTRY COUNT: 53
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5455240	A	19951003	(199546)*		18
WO 9535112	A2	19951228	(199606)	EN	46
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB HU IS JP KP KR KZ LK LU LV MG MN MW MX NO NZ PL PT RO RU SD SE SG SK TM UA UG UZ VN					
AU 9527758	A	19960115	(199620)		
WO 9535112	A3	19960201	(199622)		
EP 762884	A1	19970319	(199716)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 10504535	W	19980506	(199828)		46
KR 97703775	A	19970809	(199836)		
AU 701347	B	19990128	(199916)		
MX 9700037	A1	19990401	(200055)		
MX 199300	B	20001027	(200212)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5455240	A	US 1994-262306	19940620

WO 9535112	A2	WO 1995-US7687	19950619
AU 9527758	A	AU 1995-27758	19950619
WO 9535112	A3	WO 1995-US7687	19950619
EP 762884	A1	EP 1995-923082	19950619
		WO 1995-US7687	19950619
JP 10504535	W	WO 1995-US7687	19950619
		JP 1996-502513	19950619
KR 97703775	A	WO 1995-US7687	19950619
		KR 1996-707289	19961219
AU 701347	B	AU 1995-27758	19950619
MX 9700037	A1	MX 1997-37	19970107
MX 199300	B	MX 1997-37	19950619

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9527758	A	Based on	WO 9535112
EP 762884	A1	Based on	WO 9535112
JP 10504535	W	Based on	WO 9535112
KR 97703775	A	Based on	WO 9535112
AU 701347	B	Previous Publ.	AU 9527758
		Based on	WO 9535112

PRIORITY APPLN. INFO: US 1994-262306 19940620
AN 1995-357434 [46] WPIDS
AB US 5455240 A UPAB: 19951122
A method for preventing or **treating** an infection with **Streptococcus pneumoniae** (SP) comprises administering to a subject an **antagonist** of platelet activating factor (PAF) receptor to inhibit binding of SP to host cells.

USE - The method and compsn. are used for treating or preventing S.P. infection.

ADVANTAGE - Inhibition of the binding of SP to the PAF receptor prevents migration of pneumococci across epithelial and endothelial tissues which can lead to a systemic bacterial infection, resulting in bacteremia, sepsis and meningitis. In addn., inhibition of the binding can prevent activation and inflammation.

Dwg.0/6

L10 ANSWER 32 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1989:301179 BIOSIS
DOCUMENT NUMBER: BR37:15556
TITLE: EFFECT OF LEUKOTRIENE **ANTAGONIST** FPL-57231 ON CARDIOPULMONARY FUNCTION IN PIGLETS **TREATED** WITH GROUP B **STREPTOCOCCAL** GBS EXOTOXIN TOX.
AUTHOR(S): OSIOVICH H; GOLDBERG R N; SUGUIHARA C; HELLERQVIST C G; HEHRE D; BANCALARI E
CORPORATE SOURCE: DEP. PEDIATR., DIV. NEONATOLOGY, UNIV. MIAMI, MIAMI, FLA.
SOURCE: JOINT MEETING OF THE AMERICAN PEDIATRIC SOCIETY AND THE SOCIETY FOR PEDIATRIC RESEARCH, WASHINGTON, D.C., USA, MAY 1-4, 1989. PEDIATR RES, (1989) 25 (4 PART 2), 279A.
CODEN: PEREBL. ISSN: 0031-3998.
FILE SEGMENT: BR; OLD

LANGUAGE: English

L10 ANSWER 33 OF 34 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 89:197280 SCISEARCH
THE GENUINE ARTICLE: T9471
TITLE: EFFECT OF LEUKOTRIENE **ANTAGONIST** FPL 57231 (FPL) ON CARDIOPULMONARY FUNCTION IN PIGLETS **TREATED** WITH GROUP-B **STREPTOCOCCAL** (GBS) EXOTOXIN (TOX)
AUTHOR: OSIOVICH H (Reprint); GOLDBERG R N; SUGUIHARA C; HELLERQVIST C G; HEHRE D; BANCALARI E
CORPORATE SOURCE: UNIV MIAMI, DEPT PEDIAT, DIV NEONATOL, MIAMI, FL, 33152; VANDERBILT UNIV, NASHVILLE, TN, 37240
COUNTRY OF AUTHOR: USA
SOURCE: PEDIATRIC RESEARCH, (1989) Vol. 25, No. 4, pp. A279.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L10 ANSWER 34 OF 34 MEDLINE
ACCESSION NUMBER: 62035973 MEDLINE
DOCUMENT NUMBER: 62035973
TITLE: **Antagonistic** effect of a penicillinase-producing staphylococcus on penicillin **therapy** of a **streptococcal** throat infection.
AUTHOR: FRANK P F; MILLER L F
SOURCE: Amer J Med Sci, (1962 May) 243 582-5.
DOCUMENT TYPE: Journal
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE
ENTRY MONTH: 196212
ENTRY DATE: Entered STN: 19990716
Last Updated on STN: 19990716

[redacted] (FILE 'USPATFULL' ENTERED AT 10:59:18 ON 05 SEP 2002)
L7 7899 SEA ((STREPTOCOCC? OR S)(W) PNEUMON? OR STREPTOCOC?)(5A)(TREAT? OR THERAP?)
L12 4 SEA FILE=USPATFULL ABB=ON PLU=ON L7(S)ANTAGONIST?

L12 ANSWER 1 OF 4 USPATFULL
ACCESSION NUMBER: 2002:192034 USPATFULL
TITLE: Methods using the SRP polynucleotides and polypeptides and compounds modulating their activity
INVENTOR(S): Cheever, Christy, Strafford, PA, UNITED STATES
Fecteau, Douglas A., Conshohocken, PA, UNITED STATES
Li, Hu, Eagleville, PA, UNITED STATES
Payne, David J., Phoenixville, PA, UNITED STATES
Steel, Angela, Chester Springs, PA, UNITED STATES
Wang, Lei, Conshohocken, PA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002103104	A1	20020801	
APPLICATION INFO.:	US 2001-814041	A1	20010320	(9)

Searcher : Shears 308-4994

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-191008P	20000321 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edward R. Gimmi, SmithKline Beecham Corporation, Corporate Intellectual Property-U.S., UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 1563
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods for RNA screening for antimicrobial compounds using ffh polypeptides and DNA (RNA) encoding ffh polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing ffh polypeptides to screen for antibacterial compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/001.000
INCLS: 530/350.000
NCL NCLM: 514/001.000
NCLS: 530/350.000

L12 ANSWER 2 OF 4 USPATFULL
ACCESSION NUMBER: 2002:185277 USPATFULL
TITLE: Methods for treating IL-18 mediated disorders
INVENTOR(S): Sims, John E., Seattle, WA, UNITED STATES
Mohler, Kendall M., Poulsbo, WA, UNITED STATES
Born, Teresa L., Kenmore, WA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002098185	A1	20020725	
APPLICATION INFO.:	US 2002-981421	A1	20020118	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-241408P	20001018 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: IMMUNEX CORPORATION, LAW DEPARTMENT, 51 UNIVERSITY STREET, SEATTLE, WA, 98101
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention pertains to methods for treating medical disorders characterized by elevated levels or abnormal expression of IL-18 by administering an IL-18 antagonist, such as soluble IL-18 receptor, a soluble IL-18 binding protein and/or an antibody.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/145.100
INCLS: 514/009.000; 514/167.000; 514/171.000; 514/162.000;

514/251.000; 514/725.000; 514/575.000
NCL NCLM: 424/145.100
NCLS: 514/009.000; 514/167.000; 514/171.000; 514/162.000; 514/251.000; 514/725.000; 514/575.000

L12 ANSWER 3 OF 4 USPATFULL

ACCESSION NUMBER:	1999:7145 USPATFULL
TITLE:	Diagnosis and treatment of infections due to Streptococci and Enterococci
INVENTOR(S):	Burnie, James Peter, Alderley Edge, United Kingdom Matthews, Ruth Christine, Alderley Edge, United Kingdom
PATENT ASSIGNEE(S):	NeuTec Pharma plc, United Kingdom (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5861157		19990119	
APPLICATION INFO.:	US 1996-687956		19960729	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1994-1689	19940128

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Caputa, Anthony C.
ASSISTANT EXAMINER:	Navarro, Mark
LEGAL REPRESENTATIVE:	Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
NUMBER OF CLAIMS:	13
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT:	2243

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a purified bacterial protein expressed during infection due to streptococci or enterococci and isolated from human sera, together with immunogenic fragments, analogs, inhibitors, antibodies and antigenic fragments specific thereto. Also provided is a DNA sequence coding for a bacterial protein or an immunogenic fragment or an analogue thereof expressed during infection due to Streptococci or Enterococci, together with homologues thereof, together with vectors, probes and inhibitors therefor. Also provided is fibronectin or an immunogenic fragment thereof or an analogue thereof or an antibody thereto or an anigen binding fragment thereof when used in a method of treatment or diagnosis of the human or animal body for infection due to Streptococci or Enterococci. Also provided are antibodies specific to HSP 90 or immunogenic fragments or analogues thereof for use in a method of diagnosis or treatment of the human or animal body of infection due to steptococci or enterococci due to any one of the group of S.oralis, S.gordonii, S.sanguis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/139.100
INCLS: 424/190.100; 435/069.300; 530/300.000; 530/350.000; 536/023.700

NCL NCLM: 424/139.100
NCLS: 424/190.100; 435/069.300; 530/300.000; 530/350.000; 536/023.700

L12 ANSWER 4 OF 4 USPATFULL

ACCESSION NUMBER:	95:88456 USPATFULL
TITLE:	Modulators of pneumococcal adhesion to cellular targets involving the platelet activating factor receptor, and uses thereof
INVENTOR(S):	Tuomanen, Elaine I., New York, NY, United States Cundell, Diana R., New York, NY, United States Gerard, Norma P., Dover, MA, United States
PATENT ASSIGNEE(S):	The Rockefeller University, New York, NY, United States (U.S. corporation) Beth Israel Hospital Association, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5455240		19951003	
APPLICATION INFO.:	US 1994-262306		19940620	(8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Prescott, Arthur C.
LEGAL REPRESENTATIVE:	Klauber & Jackson
NUMBER OF CLAIMS:	27
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT:	1299

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compositions and methods for preventing pneumococcal infection. In particular, the invention relates to identification of the major reception for Streptococcus pneumoniae on activated human cells, and diagnostic and therapeutic compositions and methods based thereon. In particular, the invention relates to the discovery that platelet activating factor (PAF) receptor is an adhesive ligand for pneumococcal adherence to activated lung epithelial and venous endothelial (i.e., host) cells. Accordingly, the present invention is directed to a method for preventing or **treating** an infection with **Streptococcus pneumoniae** by administering an **antagonist** of platelet activating factor receptor. The invention further relates to recognition that adherence to activated cells also involves a carbohydrate ligand found on such activated cells. Thus, a method for inhibiting pneumococcal adherence may further comprise administering an amount of carbohydrate containing an N-acetyl-D-glucosamine motif. It has been found that resting lung epithelial and venous endothelial cells bear two classes of receptors containing different carbohydrate motifs. Thus, the invention further provides for administering an amount of a second carbohydrate selected from the group consisting of a carbohydrate containing a disaccharide N-acetyl-D-galactosamine .beta.1-4Gal motif, a disaccharide N-acetyl-D-galactosamine .beta.1-3Gal motif, and a mixture thereof. In addition, the invention provides pharmaceutical compositions comprising such agents that inhibit binding of pneumococci to human cells. In a specific example, platelet activating factor receptor **antagonists** and disaccharides

are shown to inhibit binding of pneumococci to activated lung epithelial cells and venous endothelial cells, as well as cells transfected with the platelet activating factor receptor, in vitro.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/210.000
INCLS: 514/008.000; 514/025.000; 536/004.100; 536/017.400; 536/017.600; 536/021.000; 424/122.000
NCL NCLM: 514/025.000
NCLS: 424/122.000; 514/008.000; 536/004.100; 536/017.400; 536/017.600; 536/021.000

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 11:00:10 ON 05 SEP 2002)
L13 2975 S GILBERT C?/AU
L14 61 S HANSBRO P?/AU
L15 2 S L13 AND L14
L16 3034 S L13 OR L14
L17 4 S L16 AND L1
L18 4 S L15 OR L17
L19 3 DUP REM L18 (1 DUPLICATE REMOVED)

- Author (s)

L19 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:98775 HCAPLUS
DOCUMENT NUMBER: 132:162046
TITLE: Sequences of **Streptococcus pneumoniae** proteins and nucleic acid molecules, and uses thereof in in drug screening, diagnostic, and **therapeutic** applications
INVENTOR(S): **Gilbert, Christophe Francois Guy; Hansbro, Philip Michael**
PATENT ASSIGNEE(S): Microbial Technics Limited, UK
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006737	A2	20000210	WO 1999-GB2451	19990727
WO 2000006737	A3	20000629		
W: CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1100921	A2	20010523	EP 1999-934989	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-16337 A 19980727
US 1999-125164P P 19990319
WO 1999-GB2451 W 19990727

AB The invention provides sequences of novel protein antigens from type 4 Streptococcus pneumoniae. The invention also provides for the use of the disclosed nucleic acids/proteins as antigens/immunogens, in the diagnosis of Streptococcus infections, and in screening for

potential antimicrobial agents.

L19 ANSWER 2 OF 3 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-656168 [63] WPIDS
CROSS REFERENCE: 2001-451553 [48]
DOC. NO. NON-CPI: N2000-486434
DOC. NO. CPI: C2000-198585
TITLE: Novel antigens from **Streptococcus pneumoniae** of specific molecular weights useful for **treatment**, prophylaxis and diagnosis of **Streptococcus pneumoniae** infections.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): CRIPPS, A W; **HANSBRO, P M**; JOMAA, M; KYD, J M; WELLS, J M
PATENT ASSIGNEE(S): (PROV-N) PROVALIS UK LTD
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000058475	A2	20001005	(200063)*	EN	45
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CN JP US					
EP 1165795	A2	20020102	(200209)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1345375	A	20020417	(200248)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000058475	A2	WO 2000-GB1167	20000327
EP 1165795	A2	EP 2000-912834	20000327
		WO 2000-GB1167	20000327
CN 1345375	A	CN 2000-805589	20000327

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1165795	A2	Based on	WO 200058475

PRIORITY APPLN. INFO: GB 1999-28678 19991203; GB 1999-7114 19990326
AN 2000-656168 [63] WPIDS
CR 2001-451553 [48]
AB WO 200058475 A UPAB: 20020730
NOVELTY - A protein or polypeptide (I) obtained from Streptococcus pneumoniae and having specific molecular weight as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and specific N-terminal sequences, is new.
DETAILED DESCRIPTION - A protein or polypeptide (I) obtained from Streptococcus pneumoniae and having specific molecular weight as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and specific N-terminal sequences, is new. (I) has a molecular weight of 55, 50, 85, 38, 30, 32, 43 or 100 kDa, and has an N-terminal sequence of ValGluProLysAlaLysProAlaAspPr

oSerValVal, AsnAspArgLeuValAlaThrGlnSerAlaAspGlyArgAsnGluSerValLeuMe
tSerIleGluThr, GluAspThrThrAsnSerArgPheGlySerGlnPheAspLysTyrArgGlnPr
oAsnAlaGlnProAspHisSerHisAspAlaValSerAlaAspAsnSerThrAlaHisAsnArgPheG
lyTyrGlyPheAlaIleGlySerLysTyrIleArgTyr,
AspLysTyrArgGlnProAsnAlaGluProAspAspHisHisTyrAlaVal,
AspAlaValSerAlaAsp or SerGluThrAsnValTyr,
AspLysValAspGluLeuSerAlaLysProAspIleLeuLysPro,
GluLeuLysGluGluGly(Trp)ValValLys, and GluValHisAla, respectively.
Alternatively, (I) has a molecular weight of less than 14 kDa as determined by SDS-PAGE, and an N-terminal sequence of MetLysLeuAsnGluValLysGluPheValLysGluLeuArgAlaGluThr, AlaLysTyrGluIleLeuTyrIleGluArgProAsnIleGluGluPheAlaLys or Ile(Arg)LeuThrArgMet(Glu)GlyGlyLysLysLysPro(Lys)PheTyrTyr, or has a molecular weight of 16, 27.5, 44 or 12-14 kDa which have a N-terminal sequence of ValMetThrAspProIleAlaAspXLeuXArgIle, (ValAla)(LysGlu)LeuValPheAlaArgHisGlyGlu(LeuThr)Glu(AsnLys), IleIleThrAspValTyrAlaArgGluValLeuAspSerArgGlyAsnProThrLeu, and AlaLeuAsnIleGluAsnIleIleAlaGluIleLysIleAlaSer, respectively. (I) is a reduced toxicity variant or fragment of the above mentioned proteins, preferably has a molecular weight of 16 or 57 kDa under reducing conditions and has the following N-terminal sequence of ArgIleIleLysPheValTyrAlaLys.

INDEPENDENT CLAIMS are also included for the following:

(1) a homologue or derivative (II) of (I);

(2) one or more antigenic fragments (III) of (I) or (II);

(3) a nucleic acid molecule (IV) comprising or consisting of a DNA sequence encoding for (I) or their RNA equivalents, a sequence which is complementary or substantially identical to the sequence, or a sequence which codes for (II) or (III);

(4) a vector (V) comprising (IV);

(5) a host cell (VI) comprising (V);

(6) an immunogenic/antigenic composition (VII) comprising (I), (II) or (III);

(7) a vaccine composition (VIII) comprising (IV);

(8) an antibody (IX) raised against and/or binding to (I), (II) or (III);

(9) a kit for detecting/diagnosing S. pneumoniae infection comprising (I), (II), (III) or (VII);

(10) a kit for detecting/diagnosing S. pneumoniae infection comprising (IV);

(11) determining if (I) represents a potential anti-microbial target involves inactivating the protein or polypeptide, and determining if S. pneumoniae is still viable, in vitro or in vivo;

(12) use of an agent capable of antagonizing, inhibiting or otherwise interfering with the function or expression of (I) in the manufacture of a medicament for use in **treatment** or prophylaxis of **S. pneumoniae** infection; and

(13) preparation of (I).

ACTIVITY - Antibacterial. Balb/c mice, 6-10 weeks old were immunized with the immunization protein, prepared by emulsifying 2.5 micro g/ micro L protein in a 1:1 ratio with incomplete Freund's adjuvant on day 0 by Peyer's patches inoculation and boosted by intratracheal administration 14 days later. On day 21, these mice were challenged with live Streptococcus pneumoniae. Blood was collected, the trachea was exposed and the lung were lavaged by insertion and removal of 0.5 mL sterile phosphate buffered saline (PBS). The recovered fluid (BAL) was assessed for bacterial recovery by plating 10 fold serial dilutions onto blood agar for colony

forming units (CFU) determination. The lungs were removed following lavage, placed in 2 mL sterile PBS and homogenized. The lung homogenate was assessed by plating 10-fold serial dilutions onto blood agar for CFU determination. Three proteins assessed in immunization and bacterial challenge showed significant degrees of pulmonary clearance from the lungs. These were proteins with molecular masses of 16, 34 and 57 kDa. A fourth protein of significance was the 12-14 kDa protein which is a toxin and potential virulence component of S. pneumoniae.

MECHANISM OF ACTION - Vaccine; gene therapy.

USE - (I), (II), (III), (IV) or (IX) is useful for detection/diagnosis of **S. pneumoniae**. (I), (II), (III), (IV) or (VII) is useful for vaccinating a subject against **S. pneumoniae**. The novel polypeptides, its derivatives or homologs and the nucleic acid molecules are useful in **treatment** or prophylaxis of **S. pneumoniae** infection. (All claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the flow chart of the protein purification procedure.

Dwg.2/8

L19 ANSWER 3 OF 3 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-195301 [17] WPIDS
DOC. NO. NON-CPI: N2000-144461
DOC. NO. CPI: C2000-060591
TITLE: **Streptococcal** proteins and polynucleotides useful for diagnosis, **treatment** and prophylaxis of bacterial infections.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HANNIFFY, S B; **HANSBRO, P M**; LE PAGE, R W F; WELLS, J M
PATENT ASSIGNEE(S): (MICR-N) MICROBIAL TECHNICS LTD
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000006738	A2	20000210	(200017)*	EN	76
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CN JP US					
EP 1144640	A2	20011017	(200169)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1318103	A	20011017	(200213)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000006738	A2	WO 1999-GB2452	19990727
EP 1144640	A2	EP 1999-934990	19990727
		WO 1999-GB2452	19990727
CN 1318103	A	CN 1999-810978	19990727

FILING DETAILS:

PATENT NO	KIND	PATENT NO

EP 1144640 A2 Based on WO 200006738

PRIORITY APPLN. INFO: US 1999-125329P 19990319; GB 1998-16336 19980727

AN 2000-195301 [17] WPIDS

AB WO 200006738 A UPAB: 20000405

NOVELTY - Streptococcus pneumoniae protein or polypeptide (I), its homologs or derivatives, with a fully defined sequence amino acids (given in the specification), is new.

DETAILED DESCRIPTION - (I) has an amino acid sequence selected from 12 sequences given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) a protein or polypeptide (II), its homologs or derivatives having a defined amino acid sequence selected from 61 sequences given in the specification;

(2) an antigenic and/or immunogenic fragment of (I), (II) or a protein or polypeptide (III) having a sequence selected from 12 sequences of defined amino acids given in the specification;

(3) a nucleic acid molecule (IV) encoding (I), (II) or (III) having defined DNA sequences given in the specification (or their RNA equivalents, complementary sequences, homologs, derivatives or identical sequences);

(4) an immunogenic and/or antigenic composition (V) comprising (I), (II) or (III) or homologs, derivatives and/or fragments;

(5) a vaccine composition comprising (III);

(6) an antibody (VI) capable of binding to (I), (II), (III) or a homolog, derivative or fragment; and

(7) determining the anti-microbial activity of (I) (II) and (III) by inactivating the protein and determining the viability of S.pneumoniae.

ACTIVITY - Antiinflammatory; antibacterial.

MECHANISM OF ACTION - Vaccine; antagonist.

100 micro g of recombinant pcDNA3.1 (IV) was injected intramuscularly into the tibialis anterior muscle of both legs of mice. A booster dose was given 4 weeks later and control groups received either non-recombinant pcDNA3.1+DNA or no vaccine. After the second immunization, all mice groups were challenged intra-nasally with a lethal doses of Streptococcus pneumoniae serotype 4 (strain NCTC 11886). Mice were monitored for the development of symptoms associated with the onset of S.pneumoniae induced-disease. The groups vaccinated with DNA survived significantly longer than non-vaccinated controls.

USE - (I) or homologs, derivatives and/or fragments are useful as an immunogen or antigen and (V) is useful as a vaccine and also in a diagnostic assay. (I-V) are useful for detection or diagnosis of **S. pneumoniae**, by contacting a sample to be tested with them. Agents capable of antagonizing, inhibiting or interfering with the function or expression of the protein or polypeptide (II) are useful in medical compositions in the **treatment** or prophylaxis of **S.pneumoniae** infection (claimed).

Dwg.0/2

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